"CLINICAL AND ECHOCARDIOGRAPHIC PREDICTORS OF IN-HOSPITAL MORTALITY IN ST ELEVATION MYOCARDIAL INFARCTION"

Dissertation submitted for

D.M. DEGREE EXAMINATION
BRANCH II – CARDIOLOGY

MADRAS MEDICAL COLLEGE
AND
GOVERNMENT GENERAL HOSPITAL
CHENNAI – 600 003

THE TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY
CHENNAI – 600 032
AUGUST 2008

CERTIFICATE

This is to certify that the dissertation entitled **"CLINICAL AND ECHOCARDIOGRAPHIC PREDICTORS OF IN-HOSPITAL MORTALITY IN ST ELEVATION MYOCARDIAL INFARCTION"** is the bonafide original work of **DR.V. RAJA** in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2008.The period of post-graduate study and training was from August 2005 to July 2008.

PROFESSOR R.ALAGESAN M.D., D.M.
PROFESSOR AND HEAD OF THE DEPARTMENT OF CARDIOLOGY
MADRAS MEDICAL COLLEGE AND
GOVERNMENT GENERAL HOSPITAL
CHENNAI - 600 003.

THE DEAN
MADRAS MEDICAL COLLEGE AND
GOVERNMENT GENERAL HOSPITAL
CHENNAI - 600 003.

DECLARATION

I **Dr.V.RAJA**, solemnly declare that this dissertation entitled,**"CLINICAL AND ECHOCARDIOGRAPHIC PREDICTORS OF IN-HOSPITAL MORTALITY IN ST ELEVATION MYOCARDIAL INFARCTION"** is a bonafide work done by me at the department of Cardiology, Madras Medical College and Government General Hospital during the period 2005 – 2008 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor R.Alagesan M.D.D.M. This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of **D.M. Degree (Branch-II) in Cardiology.**

Place : Chennai
Date:

Dr.V.RAJA

ACKNOWLEDGEMENTS

A great many people made this work possible. I thank the Dean for permitting me to carry out this study.

My greatest respects and sincere gratitude to **Prof R.Alagesan MD, DM**. Professor and Head of the Department of Cardiology, Government General Hospital, Chennai who was the driving force behind this study. But for his constant guidance this study would not have been possible.

I am indebted to Prof. Geetha Subramanian, Prof A.Balaguru, Prof. B.Ramamurthy, Prof. P.Arunachalam and Prof V.E.Dhanda pani without whom, much of this work would not have been possible.

I acknowledge Dr M.A.Rajasekar for the many useful comments he made during this project.

My respectful thanks to Dr. G.Gnanavelu, Dr.D.Muthukumar for their constructive ideas, personal guidance and involvement in this study.

I am grateful to Dr.K.Meenakshi Dr.G.Karthikeyan, Dr.P.S.Mohanamurugan, Dr S.Venkatesan, Dr.G.Ravishankar, Dr.G.JustinPaul, Dr.C.Elangovan, Dr.G. Prathap Kumar for their valuable suggestions and critical appraisal of this study.

I am thankful to all those patients for their genuine cooperation.

“learn to heal”

CLINICAL AND ECHOCARDIOGRAPHIC PREDICTORS OF IN-HOSPITAL MORTALITY IN ST ELEVATION MYOCARDIAL INFARCTION

CONTENTS

INTRODUCTION

Mortality from Acute Myocardial Infarction (AMI) is said to be declining. The decline in mortality has been ascribed to a combination of community-wide preventive strategies and improved treatment.

The advent of mobile CCU, increased use of thrombolysis (including pre-hospital thrombolysis), Intensive Coronary Care and early interventional procedures have all been highlighted for the 'decline' in morbidity and mortality.(1)

Recent large scale randomized controlled thrombolytic trials have reported 30 day mortalities of 6–10% with mortality as low as 2.5% in trials of primary angioplasty (2).

But in actual clinical practice, many patients do not receive optimal treatment, including thrombolysis. Series from North America and Europe suggest that thrombolysis rates are in the region of 25%. (8, 9)

In addition, many patients are not managed in coronary care units and many are elderly. Thus the hospital mortality of unselected patients with acute myocardial infarction may be considerably higher than suggested by the results of large scale trials of thrombolysis and primary angioplasty.

Hence AMI still remains as one of the main causes of morbidity and mortality.

A number of multivariable prognostic models have been developed in populations of patients with ST-segment elevation acute myocardial infarction. Considerable variability exists in the risk for adverse events across the spectrum of ACS especially, in ST elevation MI (STEMI).

Different presenting characteristics, in large part related to identification of varying levels of risk, have become important factors in deciding on the level of care and choice of interventional and medical therapies.

This scenario necessitates an in depth analysis of predictors of in hospital mortality in AMI.

AIM OF THE STUDY

It is an enigma why some patients with AMI succumb to the disease while others survive despite almost similar features and management protocols.

Most models of predictors of mortality have been derived from databases from clinical trials, which tend to exclude high-risk patients and are not fully representative of the broad spectrum of patients encountered in general clinical practice.

Other predictive models have been developed, which may also be limited by selective bias of inclusion criteria.

Some of the most robust predictors of mortality have been developed in the selected population of patients with ST-segment elevation myocardial infarction treated with fibrinolytic therapy, and these models may not be relevant to most patients seen in practice.

Thus earlier studies have elucidated many possible predictors. However the value of such studies varies in its universal applicability.

Hence it is necessary to determine factors that are predictive of death across the entire spectrum of an unselected population of AMI patients.

In addition it remains imperative that, parameters that predict mortality be evaluated based on clinical features as well as simple and easily available investigations.

Hence it is mandatory to analyze such clinical parameters that are more uniformly acceptable and tenable as predictors of in-hospital mortality.

In addition presently echocardiographic evaluation is widely used in acute coronary

events for diagnosis and management.

However, the utilization of echocardiography as a prognostic indicator remains as an area for study and analysis.

Hence it is an important purpose of this study is to identify findings on early echocardiograms that are associated with mortality after AMI.

Further it is necessary to assess the interaction of such findings with treatment, and hence determine whether any of these echocardiographic features could provide insights into the survival benefit.

With routine use and availability of Tissue Doppler Imaging (TDI) at the bedside, whether analysis of prediction of mortality in AMI using TDI parameters would be an important variable in risk stratification.

Aim of this study is to evaluate the clinical and echocardiographic predictors of in-hospital mortality in acute ST elevation myocardial infarction in unselected patients admitted in Coronary Care Unit.

REVIEW OF LITERATURE

In a study of Hospital mortality of acute myocardial infarction in the thrombolytic era N G Mahon et.al..(4) Unselected patients from a centre with coronary intervention facilities, the hospital mortality of acute myocardial infarction was 18%.(Table 1) This is a reflection of the design of the study which included all ages and all hospital cases of acute myocardial infarction, not simply those admitted to coronary care.

Accordingly 30% of patients were over 75 years and mortality in this group was 30%, as opposed to 14% in those under 75(3, 5). Other studies reporting the hospital mortality of acute myocardial infarction since the introduction of thrombolysis have produced disparate results, with hospital mortalities ranging from 8.4% to 23%.

This disparity is determined by differences in study populations, with studies limited to younger ages or coronary care cases showing lower mortality than studies of unselected cases.

Distribution of risk factors

Smoking history (63%), diabetes mellitus (28%), family history (22%), and hypertension (32%) did not differ significantly from the other centre series. The occurrence of left ventricular failure (33%), ventricular arrhythmias 11%), and post infarction angina or reinfarction (15%) lower than in the tertiary centre(45%,18% and 34% respectively).

PREDICTORS OF HOSPITAL MORTALITY

These are shown in Table 2. The mean age of patients dying was 73 years v 67 years in patients surviving.(10,11) Patients age was a predictor of mortality in hospital in both univariate ($p < 0.001$) and multivariate analysis ($p < 0.001$). Other predictors of hospital mortality by univariate analysis included sex, the use of thrombolysis, and the occurrence of left ventricular failure, cardiogenic shock, ventricular arrhythmias, and heart block requiring temporary pacing. Other independent predictors of mortality following multivariate analysis were left ventricular failure, shock, ventricular arrhythmias, management outside the CCU, and the development of reinfarction.

Table 1. **Summarizes clinical and demographic features, complication rates, and outcomes of patients admitted with acute myocardial infarction**.

	*Frequency, n (%)**
Age (years) (mean (SD))	67.0 (13)
Male sex	595 (60)
Admission to coronary care	682 (70)
Infarct	
First	339 (44)
Second or more	429 (56)
Anterior	348 (38)
Inferior	380 (41)
Risk factors	
Current or former smoker	528 (59)
Diabetes mellitus	168 (18)
Family history	300 (34)
Hypertension	282 (32)
Cholesterol (mmol/l) (mean (SD))	5.3 (1.7)
Complications	
Left ventricular failure	400 (44)
Cardiogenic shock	92 (10)
Ventricular arrhythmia	157 (18)
Cardiac arrest	134 (15)
Temporary pacemaker	58 (6.5)
Permanent pacemaker	25 (2.8)
Postinfarct angina	238 (27)
Reinfarction	65 (7.4)
Atrial fibrillation (persistent)	148 (17)
Pericarditis	33 (3.7)
VSD/papillary muscle rupture	14 (1.6)
Cerebrovascular accident	30 (3.6)
DVT/pulmonary embolism	12 (1.4)
Death in hospital	190 (18.2)

*Except age and cholesterol, which are given as mean (SD).
DVT, deep venous thrombosis; VSD, ventricular septal defect.

Table 2 .**Predictors of in hospital mortality**

	*Yes, n (%)**	*No, n (%)**	*p Value (χ^2)*	*p Value (multivariate)*
Male sex	94 (14.8)	101 (23.9)	< 0.001	NS
Thrombolysis	32 (14.0)	122 (22.4)	< 0.05	NS
CCU	112 (15.0)	83 (36.0)	< 0.001	< 0.001 (0.4)†
Smoking	71 (14.6)	61 (20.8)	< 0.05	NS
Family history	29 (10.3)	96 (20.6)	< 0.001	NS
LVF	112 (31.0)	48 (10.4)	< 0.001	< 0.01 (1.7)†
Cardiogenic shock	61 (78.2)	99 (13.3)	< 0.001	< 0.001 (19)†
Ventricular arrhythmia	50 (34.3)	110 (16.3)	< 0.001	< 0.001 (3)†
AV block	26 (48.2)	135 (17.6)	< 0.001	NS
Reinfarction	26 (60.0)	132 (17.0)	< 0.001	< 0.01 (3.9)†
Age (mean)	73 years (Dead at follow up)	67 years (Alive at follow up)	< 0.001	< 0.001 (1.05)†

*n, number of patients dying in hospital with and without each listed variable; (%), proportion of those with or without the variable who died in hospital
†Odds ratio.
AV, atrioventricular; CCU, coronary care unit admission; LVF, left ventricular failure.

In this study, Thrombolytic treatment was associated with improved outcome in univariate but not multivariate analysis. (18)The major influences on the rate of thrombolysis are the presence of ECG criteria for thrombolysis and the time of presentation with acute myocardial infarction. There was also evidence for underutilization of other drug treatments. The rate of aspirin use was 83%, which is comparable with data from other centers.

Cigarette smoking was a univariate predictor of lower hospital mortality. This phenomenon has been observed in several large thrombolytic trials and may reflect younger age at presentation in smokers (mean age of smokers in this study was 65 years v 70 years in non-smokers), a lower prevalence of other risk factors, a higher proportion of arrhythmic deaths before reaching hospital, reversal of risk following cessation of smoking during the hospital admission or a better response to thrombolysis owing to the predominantly thrombotic nature of the lesion.

A family history of premature coronary disease was also associated with a better outcome. Again this reflects the younger age of patients with a family history (mean age 62

years v 70 years in the remaining population), and may be a result of earlier presentation in patients with a family history or of more difficulty in eliciting a family history from elderly patients.

The observation of a higher hospital mortality in the tertiary referral centre, where the coronary intervention rate was high, might be construed as evidence against the benefits of coronary interventions in acute myocardial infarction.(6,7)

Reports from the VANQWISH and OASIS trials, and previously from trials such as TIMI II, have questioned the benefit of coronary interventions in acute coronary syndromes and acute myocardial infarction. (19-27).

However, data from the GUSTO trial suggest higher morbidity among patients undergoing fewer interventions and a study of varying practices in 16 Kaiser Permanente hospitals showed a significant inverse correlation between higher intervention rates and mortality.

In the present study, the apparent paradox of a higher mortality in the centre with the higher intervention rates may be explained by a bias in demographics.(12,13)

The non-tertiary centre patients were considerably younger, they had fewer co morbidities, and more of these patients were managed in coronary care and received thrombolysis.

Cardiogenic Shock Complicating Acute Myocardial Infarction

While analyzing the SHOCK (SHould we emergently revascularize Occluded Coronaries in cardiogenic shock?) trial, Judith S. Hochman finds that though,the strategy of

early revascularization is superior to initial aggressive medical therapy, despite the advantages of early percutanous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG), once shock is diagnosed, the mortality rate remains high (50%), and half of the deaths occur within the first 48 hours. This may be caused by irreversible extensive myocardial or vital-organ damage.

He further suggests, that a systemic inflammatory response, complement activation, release of inflammatory cytokines, expression of inducible nitric oxide (NO) synthase (iNOS), and inappropriate vasodilation may play an important role not only in the genesis of shock but also in outcome after shock. New insights and therapies are needed.

Classic Shock Paradigm

The underlying pathophysiology of CS is profound depression of myocardial contractility, resulting in a vicious spiral of reduced cardiac output (CO), low blood pressure, further coronary insufficiency, and further reduction in contractility and CO(28). The classic paradigm predicts that compensatory systemic vasoconstriction with high systemic vascular resistance (SVR) should occur in response to the depression of CO (Figure 1).

Autopsy studies have shown that the pathological basis of CS is extensive MI. Varying pathological stages of infarction confirm the stuttering and progressive nature of the myocardial necrosis as a corollary of the vicious spiral. Combined new and old infarctions consistently involve at least 40% of the LV myocardium in these autopsy specimens.(29)

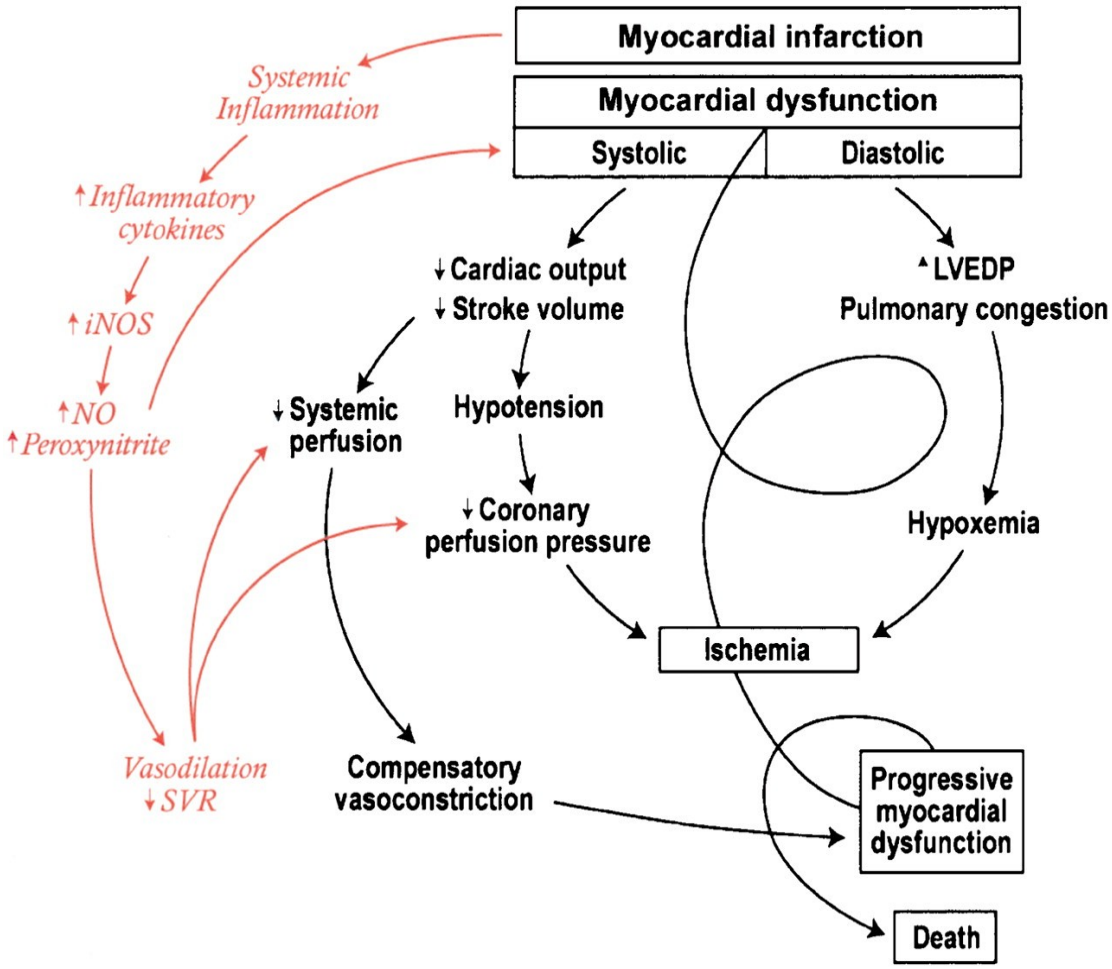


Figure 1. Classic shock paradigm, as illustrated by S. Hollenberg, is shown in black. The influence of the inflammatory response syndrome initiated by a large MI is illustrated in red. LVEDP indicates left ventricular end-diastolic pressure.

Observations That Challenge the Classic Paradigm

There are several observations derived from the SHOCK (SHould we emergently revascularize Occluded Coronaries in cardiogenic shock?) trial and registry about patients with CS due to LV failure not easily explainable by our traditional concepts. These include the following:

Average LV ejection fraction (EF) is only moderately severely depressed (30%), with a wide range of EFs and LV sizes noted.

SVR on vasopressors is not elevated on average, with a very wide range of SVRs measured.

A clinically evident systemic inflammatory response syndrome is often present in patients with CS.

Most survivors have class I congestive heart failure (CHF) status.

Surprisingly, an average EF of 30% was observed in left ventriculograms and echocardiograms obtained soon after shock diagnosis in patients with confirmed shock in the SHOCK trial. Although LV performance was measured most often on inotropic and intra-aortic balloon counterpulsation support, both of which increase EF, the hemodynamic measurements obtained concurrently document persistent hypotension, low CO, and high filling pressures.

Patients with remote MI or dilated cardiomyopathy and mild to moderate chronic CHF often have EFs considerably lower than this and are not in shock. These observations highlight the role of ventricular dilation to maintain stroke volume and peripheral vascular and neurohormonal adaptation in chronic CHF. However, an EF in the low 30s is not uncommon in uncomplicated patients with recent MI who do not have CHF.

The classic notion that acute reduction in CO leads to compensatory vasoconstriction was not confirmed in many patients in the SHOCK registry and trial (Menon et al(30) and Hochman et al,). SVR varied widely but on average was not elevated at $\approx$1350 to 1400 dyne $\cdot$ s $\cdot$ cm^{-5} despite vasopressors use.

Cotter et al(31,32) categorized acute heart failure patients according to cardiac power and demonstrated its importance in risk stratification and selection of therapy. Cardiac power, the product of cardiac index and mean arterial pressure, is a useful prognostic indicator in chronic heart failure. Acute heart failure patients with very high SVR and reduced CO have high cardiac power indices, in contrast to most shock patients, who have low cardiac power.

In both the SHOCK trial and the SHOCK registry, cardiac power was the hemodynamic variable most strongly associated with mortality. A small subset of patients in the SHOCK registry was clinically diagnosed with CS without hypotension based on systemic hypoperfusion, low CO, and elevated ventricular filling pressures. In these patients, blood pressure was maintained by elevated SVR. Their in-hospital mortality rate (although high at 43%) was lower than the rate of those patients with classic hypotensive shock (66%), despite the 2 groups having the same LVEF (34%), cardiac index (1.9 L/min per m^2), and pulmonary capillary wedge pressure (25 mm Hg).

The ability to vasoconstrict vascular beds that supply nonvital organs is an important compensatory response to a reduction in CO. Vasodilators (endogenous and exogenous) interferes with this critical response, which is needed to maintain flow to the cerebral and coronary circulations. Cardiac power is also prognostically important because it reflects myocardial reserve adequate to generate flow, albeit reduced, in the face of high resistance.

A clinically overt systemic inflammatory response syndrome as evidenced by fever, elevated white blood cell count, and low SVR, was observed in many patients with confirmed shock complicating acute MI in the randomized SHOCK trial. These findings often led to a secondary clinical diagnosis of suspected sepsis. However, the low SVR despite vasopressors was documented at shock onset, days before sepsis was suspected.(33)

The classic notion that CS develops when 40% of the LV is irreversibly damaged is inconsistent with the following observations:

(1) Survival of 50% of patients, who undergo early revascularization,

(2) Evidence of improved EF in some patients following revascularization, and

(3) New York Heart Association CHF class I for 58% of patients after shock.

Resolution of severe ischemia and/or neurohormonal-inflammatory abnormalities explains the complete reversibility of the shock state in some patients. The wide variation in EF, LV size, and SVR in the SHOCK trial suggests that the pathophysiology of shock varies among patients.

A New Paradigm

A systemic inflammatory response syndrome occurs in the setting of a number of noninfectious, major systemic insults, including trauma, cardiopulmonary bypass, pancreatitis, and burns. Patients with large MIs often have elevation of body temperature, white blood cell count, complement, interleukins, C-reactive protein, and other inflammatory markers. NO, synthesized at low levels by endothelial and myocardial cell endothelial nitric oxide (eNOS), is a cardio protective molecule.(33,34)

In contrast, many cell types express iNOS at pathological levels after trauma or exposure to inflammatory mediators (ie, bacterial lipopolysaccharide, tumor necrosis factor-α, and interleukin-1). Such expression may lead to toxic levels of NO and the cytotoxic NO-derived species, peroxynitrite, formed by reaction with superoxide. In experimental models, high iNOS and NO levels are seen after MI and subsequent reperfusion. Release of cytokines by the heart

after MI has been documented in patients. These levels markedly increase after primary PCI in acute MI patients but not in control patients.

This suggests that in patients post-MI, activation of inflammatory cytokines leads to high levels of iNOS, NO, and peroxynitrite, all of which have multiple deleterious effects.

Effects of High Levels of NO and NO-Derived Species (eg, Peroxynitrite)

Direct inhibition of myocardial contractility
Suppression of mitochondrial respiration in nonischemic myocardium
Effects on glucose metabolism
Proinflammatory effects
Reduced catecholamine responsivity
Induction of systemic vasodilation

The mechanism of the detrimental effect of high NO levels is unclear, but it may result from a direct effect of NO on myocardial contractility by uncoupling of calcium metabolism, (35 ,36)through effects on glucose metabolism, or through ß-adrenergic responsivity.(37) High levels of iNOS are associated with LV dysfunction and higher mortality in mice with MIs. (38,39).

In animal models, NO production by iNOS is deleterious during ischemia-reperfusion. (35,36) Induced iNOS expression and high NO levels during ischemia may mediate myocardial stunning. Furthermore, stimulation of iNOS expression by interleukins could explain the observation of new or worsening hypotension after primary PCI in some patients.

A marked variability in the responsiveness of the inflammatory system has been reported, supporting the concept that systemic inflammation may play a large role in some patients but not in others in the genesis and persistence of shock. Liuzzo et al reported an enhanced inflammatory response to PCI in patients with severe unstable angina that was highly variable and related to baseline, pre-PCI levels of interleukin-6 and C-reactive protein.

In patients with acute coronary syndrome, elevated inflammatory markers, including white blood cell count and C-reactive protein, are independently associated with mortality.

Beneficial Effects of Inhibiting Inflammatory Mediators and Inos

Experimentally, iNOS knockout mice were shown to survive MI better than wild-type mice. In ischemia-reperfusion models, inhibition of NO synthase appears to have favorable metabolic, antistunning, and coronary blood flow effects.

Cotter and colleagues administered a non–isoform-specific NOS inhibitor, N^G-monomethyl-L-arginine (L-NMMA), to 11 patients with persistent shock despite vasopressors, intra-aortic balloon pump, and PCI. Urine output and blood pressure increased markedly, and 72% survived to 30 days.

Cotter et al subsequently reported a reduction in 30-day mortality from 67% to 27% with a similar NOS inhibitor, N^G-nitro-L-arginine methyl ester, in a small randomized trial of 30 patients.

Inhibition of the complement cascade at the C5 level results in, among other effects, a reduction of the excess iNOS response to ischemia and reperfusion and could theoretically inhibit the genesis of shock.

Preliminary results of the COMplement inhibition in Myocardial infarction treated with Angioplasty (COMMA) study demonstrate that inhibition of C5 was associated with lower rates of shock and death in high-risk patients undergoing primary PCI, despite an absence of effect on infarct size.

In the randomized SHOCK trial, a strategy of early revascularization resulted in 132

lives saved at 1 year per 1000 patients treated as compared with initial medical therapy followed by no or late revascularization as clinically determined. This magnitude of benefit is comparable to that of CABG versus medical therapy for patients with left main coronary stenoses. Recommended selection of initial reperfusion for CS is outlined in Figure 2.

Most patients in the SHOCK trial had severe multivessel disease, and of those revascularized in the early revascularization group of the SHOCK trial, 40% underwent CABG. This is in marked contrast to the low and decreasing rate of CABG for shock in the National Registry of Myocardial Infarction (NRMI).

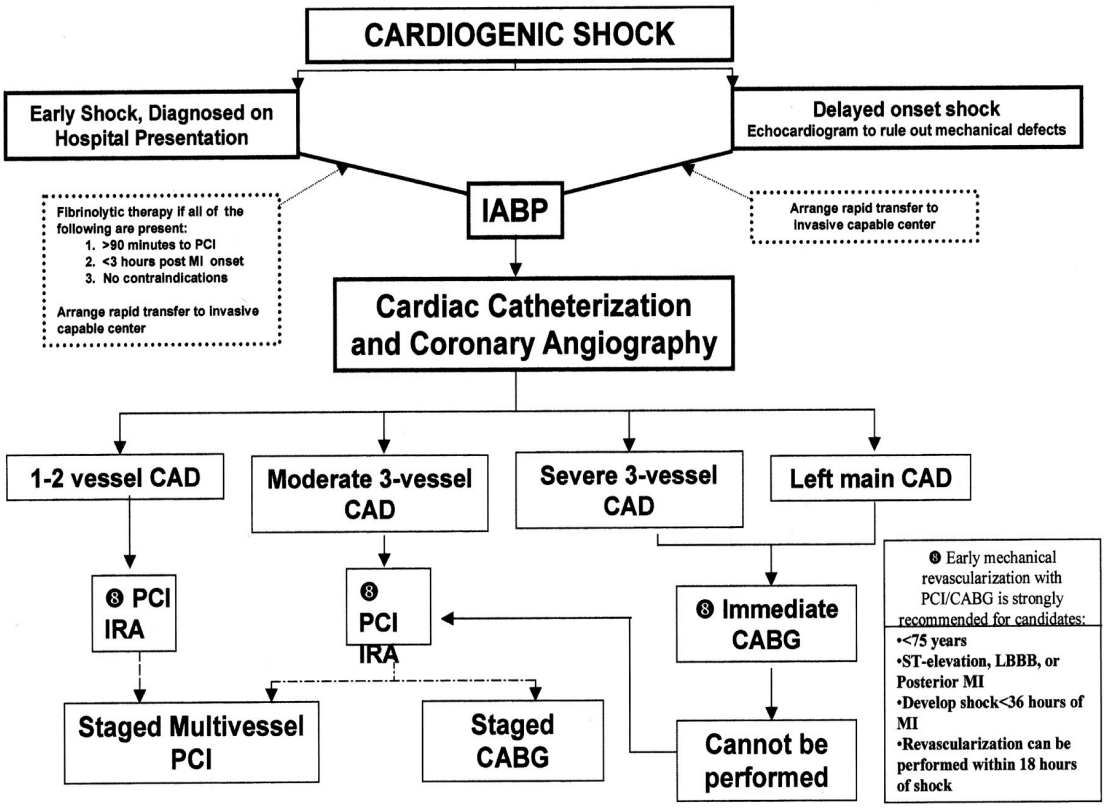


Figure 2. Recommendations for initial reperfusion therapy when CS complicates acute MI. Early mechanical revascularization with PCI or CABG is strongly recommended for suitable candidates <75 years of age and for selected elderly patients. Dashed lines indicate that the procedure should be performed in patients with specific indications only. Recommendations for staged CABG and multivessel PCI are discussed in the text, as are definitions of moderate and severe 3-vessel CAD. LBBB indicates left bundle-branch block.

The preferred treatment is PCI of the IRA for patients with 1- to 2-vessel coronary artery disease (CAD) and suitable lesions. Moderate 3-vessel disease, ie, 100% IRA occlusion, <90%

stenosis in 2 other major vessels, or more severe lesions in second-order vessels, may be treated with PCI of the IRA and staged complete revascularization, as indicated. Glycoprotein IIb/IIIa antagonists and stents are recommended.

Immediate CABG is the preferred treatment for severe 3-vessel or left main CAD. If CABG cannot be performed, single-vessel or multivessel PCI may be attempted. Distal embolization in the non–IRA territories during PCI may be disproportionately harmful in the setting of shock or recent shock.

Therefore, CABG is generally preferred to PCI when revascularization of the non–IRA artery is clinically indicated in the week after shock. However, early multivessel PCI may be warranted when shock persists despite PCI of the IRA, when CABG cannot be performed.

Echocardiographic Predictors of Survival and Response to Early Revascularization in Cardiogenic Shock -Sub study of SHOCK trial

From 1993 to 1998, 302 acute MI patients at 30 sites were randomized within 12 hours of cardiogenic shock diagnosis to either early emergency revascularization (ERV) or initial medical stabilization (IMS).

Echocardiography

During the 4 years of the trial, 2D transthoracic echocardiograms were performed on each patient within 24 hours of randomization and predischarge The qualitative review included a complete evaluation of size and function of each ventricle and all valves in addition to LV regional wall motion assessment. Regional wall motion was scored by a 20-segment model with hyperkinetic segments graded as 0, normal as 1, mild hypokinesis as 1.5, moderate hypokinesis as 2.0, severe hypokinesis as 2.5, and akinesis/dyskinesis as 3. A total score for

regional wall motion was calculated as the sum of all segment scores. Separate scores were calculated for infarct and remote zones. A wall-motion score index was calculated by dividing the wall-motion score by number of segments visualized. Color Doppler of MR was graded with a 0 to 4 scale (0=none, 1=mild, 2=moderate, 3=moderate to severe, and 4= severe). Mitral valve leaflet geometry and morphology were assessed for presence of leaflet prolapse, flail, and incomplete closure.

Quantitative analysis included right and left atrial dimensions, LV dimensions, LV volume, LV ejection fraction (EF), RV function, extent of LV endocardium involved by wall-motion abnormality, LV sphericity index, and mitral valve annular dimensions. LV volumes were measured by the method of discs from orthogonal apical views. The sphericity index was calculated as a ratio of the LV midventricular dimension (in the apical 4-chamber view) and the long-axis dimension. Doppler indices of LV filling were obtained from pulse-wave Doppler at the tips of the mitral valve and included E- and A-wave peak velocities, time velocity integrals, acceleration time, and deceleration time. RV function was measured both by the descent of the base method and as an area change.

Table 3.Characteristics of Trial Patients with Early Echocardiograms

Characteristics	ERV (n=82)	IMS (n=87)
Age, y	65±10	65±12
Male, %	70	76
Transfer admission, %	62	64
Median time, h	4.9	5.0
MI to shock		
MI to randomization	10.8	12.1
Randomization to Echo	0.2	0.6
Prior MI, %	29	35
Diabetes, %	43	20
History of hypertension, %	49	42
History of CHF , %	3.8	4.8
Renal insufficiency, %	9.6	4.9
Prior CABG, %	1.2	9.2
Prior PTCA, %	1.0	4.7

Of the early echocardiograms suitable for analysis, 82 were from the ERV group and 87 from the IMS patients. The characteristics of the patients with early echocardiograms were similar in terms of age, sex, rate of transfer admissions, and timing of shock and the echocardiograms (Tables 3).

Although the prevalence of most risk factors was similar, diabetes was more frequently noted in the ERV group, whereas more subjects in the IMS group had prior CABG. As seen with all 302 patients in the trial, a difference in 30-day mortality was noted in favor of ERV,

but this did not meet statistical significance. Similar to the entire trial population, at 6 months and 1 year, there was an absolute difference in survival between groups. However, this did not reach statistical significance in this smaller subset of patients.

Cardiac Structure and Function in Acute Cardiogenic Shock

The findings of the early echocardiogram showed (Table 4) mean LVEF was 31±11%. No significant differences in LV size or function were noted between the 2 groups. RV function was diminished in both groups

The wall-motion scores reflect significant regional dysfunction in both groups. No differences were observed between treatments. Regional function in the infarct zone was markedly impaired, with a mean segmental score approaching 3 (representative of akinesis/dyskinesis).

MR of grades 2+ to 4+ was noted in 39.1% of patients. The degree of MR did not differ between treatment groups (ERV mean MR grade 1.4±0.9 versus IMS 1.3±0.9). Apical displacement of mitral leaflet coaptation, also known as incomplete mitral leaflet closure pattern(40) was noted in 40% of those with grade 2+ to 4+ MR.

Table 4 .Baseline Echocardiographic Findings

Characteristics	Total (n=140)*	ERV (n=53)	IMS (n=87)
LVEDV, mL	114±43	123±48	109±39
LVESV, mL	81±36	87±39	77±34
LVEF, %	30.6±11.3	30.4±12.1	30.7±10.9
Diastolic sphericity Ix	0.50±0.09	0.51±0.09	0.49±0.09
Systolic sphericity Ix	0.46±0.11	0.46±0.10	0.46±0.11
RV area change, %	33.1±14.5	34.3±13.4	32.2±15.3
LV thrombus, %	16.8	2.8	25.4
MR grade	1.3±0.9	1.4±0.9	1.3±1.0
MR <2, %	60.9	59.1	62.0
MR ≥2, %	39.1	40.9	38.0
Total WMS	37.5±11.2	38.4±9.8	36.9±12.1
WMS index (total/No. of segments)	2.1±0.4	2.2±0.5	2.1±0.4
WMS index, infarct zone	2.6±0.3	2.6±0.3	2.6±0.3
WMS index, remote zone	0.9±0.3	0.9±0.3	0.9±0.3
Remote zone hyperkinesis, %	36.6	31.7	39.4

Echocardiographic Variables Associated With Survival

The significant echocardiographic univariate predictors of 30-day survival were LVEF and severity of MR. These same variables, as well as end-diastolic and end-systolic LV volume, were univariate predictors of 1-year survival .An LVEF cutoff of 28% is represents the median value. Furthermore, the separation of MR into those with less than grade 2+ and those with grade 2+ or higher provided the greatest discrimination between survivors and no survivors.

From the early echocardiograms, the only independent multivariate predictors of either 30-day or 1-year mortality were MR severity (MR ≥2 versus <2: 1-year odds ratio for death=6.64, *P*=0.0003) and LVEF (LVEF <28%: 1-year odds ratio for death 4.04, *P*=0.005).

Prognostic importance of tissue Doppler-derived diastolic function in patients presenting with STEMI

The present data indicate that (i) bedside Doppler echocardiography obtained on admission provides prognostic information in patients with STEMI receiving a modern therapeutic strategy and (ii) the association between *E*/*e*' ratio >15 and the long-term risk of cardiac death was independent of clinical evidence of heart failure, as well as of renal dysfunction, blood glucose level, LV systolic dysfunction, and MR.

Bedside Doppler echocardiography provides additional prognostic information over clinical and biological parameters that are routinely determined in patients presenting with STEMI. The present data advocate to perform index bedside Doppler echocardiography in the modern era of ACS management

Prognosis, clinical, and biological data in acute coronary syndrome

Both history of previous coronary events and lower glomerular-filtration rate correlated with poor prognosis in the present cohort of patients with ACS. Such observation is not unexpected since previous studies demonstrated the importance of these parameters in patients presenting with ACS.

Interestingly, higher glycemia on admission correlated with poor outcome independently from previous diabetes, as previously reported. Of note, hyperglycemia on admission predicts LV remodeling after first anterior myocardial infarction in non-diabetic patients.

Prognosis and Doppler echocardiography in acute coronary syndrome

Besides its usefulness for quantification of LV systolic function, Doppler

echocardiography provides useful information for the assessment of diastolic function and LV filling pressures.

The *E*/*e*' ratio has been well validated to assess LV filling pressures (14) The threshold of *E*/*e*' > 15 identifies at best patients with mean LV diastolic pressures above 12 mmHg measured by micromanometer-tipped catheters(14).

Raised LV filling pressures indicate a relatively load intolerant myocardium. This may results from major myocardial damage due to coronary occlusion or conversely from minor damage associated with a previous stiff LV chamber due to aging, hypertension, diabetes, or coronary atherosclerosis. These patients with increased LV filling pressures show poor outcome.(41)

The analysis of mitral inflow using pulsed Doppler signal recorded at the tips of the leaflets has a prognostic value in various cardiac diseases. Higher mitral *E*/*A* ratios and shorter deceleration times that define the restrictive pattern indicate an increased risk of adverse events after myocardial infarction.(42)

Similarly Temporelli *et al.*(43) have also observed a poor outcome in 571 patients enrolled in the GISSI-3 trial when mitral deceleration time is shortened. The propagation velocity of mitral inflow measured on M-mode colour Doppler echocardiography has also prognostic significance (44) However, reproducibility and quality of measurement of a colour M-mode slope that requires to carefully adjust the colour scale, in acute condition may be questionable in routine clinical practice.

By contrast, the direct recording of mitral annulus motion using tissue Doppler is easily obtained. The *E*/*e*' ratio gives a reasonable estimate of LV filling pressures and remains valid in

the presence of sinus tachycardia, (45)functional MR,(46) and preserved or depressed LV systolic function.(47)

Interestingly, MR was associated with cardiac death in univariate analysis. However, MR was not an independent predictor of poor outcome in contrast to Perez de Isla *et al.(48)* findings. LV dilation and dysfunction affect mitral leaflet competence thereby leading to functional MR.(49)

Functional MR in ACS might be the harbinger of LV dysfunction and could explain why the association was not found after adjustment on LV function parameters as previously suggested by Hillis *et al(50)*

Current guidelines do not recommend index echocardiogram for patients admitted for unequivocal ACS. However, bedside Doppler echocardiography may provide valuable diagnostic and prognostic information in the management of patients with acute chest pain who are admitted in intensive care

Cardiogenic Shock Complicating Acute Myocardial Infarction: Predictors of Death - GUSTO-I trial

Predictors of mortality

In the multivariable model, Killip class was the most powerful predictor, with a 2-fold increased risk for death with each worsening of class. Age had nearly the same prognostic significance, with a 1.7-fold increased risk for every 10 years.

Systolic blood pressure was the next most important variable, followed by resuscitated cardiac arrest and initial serum Creatinine level, in which a 1-mg/dL (88.4-µmol/L) increase was associated with a 1.2-fold increased risk for death. Prior aspirin (OR, 0.73; 95% CI, 0.58-0.91) and statin (OR, 0.50; 95% CI, 0.34-0.97) use was each independently associated

with lower risk for death. A few variables have been shown to be consistent, powerful predictors of risk for death in ACS.

The most important 8 factors—Killip class, age, blood pressure, resuscitated cardiac arrest, positive findings for cardiac markers, Creatinine level, ST-segment shift, and heart rate —contained most of the prognostic information.

Impact of Right Ventricular involvement on mortality and morbidity in patients with Inferior myocardial infarction- Analysis from the Collaborative Organization for RheothRx Evaluation (**CORE) trial**

Six-month mortality was 7.8% in inferior MI compared with 13.2% in anterior MI. Among patients with inferior MI, serious arrhythmias were significantly more common in patients with RV myocardial involvement who also had a trend toward higher mortality, pump failure and mechanical complications.

However, this was not associated with a difference in LV infarct size or function. A meta-analysis of six studies (n = 1,198) confirmed that RV myocardial involvement was associated with an increased risk of death (odds ratio [OR] 3.2, 95% confidence interval [CI] 2.4 to 4.1), shock (OR 3.2, 95% CI 2.4 to 3.5), ventricular tachycardia or fibrillation (OR 2.7, 95% CI 2.1 to 3.5) and atrioventricular block (OR 3.4, 95% CI 2.7 to 4.2).

Patients with inferior MI who also have RV myocardial involvement are at increased risk of death, shock and arrhythmias.(15,16) This increased risk is related to the presence of RV myocardial involvement itself rather than the extent of LV myocardial damage.

Electrocardiographic predictors of cardiogenic shock and in hospital mortality - Results From the **SHOCK Trial**

The baseline heart rate was higher in non-survivors than in survivors (106 +/- 20 versus 95 +/- 24 beats/minute, P = .001). There was a significant association between the QRS

duration and outcome in medically stabilized patients (115 +/- 28 ms in non-survivors versus 99 +/- 23 ms in survivors, P = .012), but not in emergently revascularized patients (110 +/- 31 versus 116 +/- 27 ms respectively, P = .343).

On multivariate analysis, the independent mortality predictors were increasing age, elevated pulmonary capillary wedge pressure, heart rate, sum of ST depression in medically stabilized patients, and interaction (P = .016) between a prolonged QRS duration and treatment assignment. Among patients with inferior AMI, a greater sum of ST depression was associated with poor outcome medically stabilized patients.

ECG parameters identified patients with cardiogenic shock who were at high risk. Emergency revascularization eliminated the incremental mortality risk associated with cardiogenic shock in patients with a prolonged QRS duration, or inferior AMI accompanied by precordial ST depression. Prospective assessments of the magnitude of the treatment effect based on ECG parameters are required.

High-Degree Atrioventricular Block Complicating Acute Myocardial Infarction Treated With Thrombolytic Therapy

In the prethrombolytic era, second or third degree heart block was seen in approximately 5% to 7% of patients presenting with acute MI In the setting of inferior MI, the incidence of second or third degree heart block can be as high as 28%. [(17)]

Although the advent of thrombolytic therapy has substantially decreased the mortality associated with acute MI, the incidence of AVB, particularly in the setting of inferior MI remains high, AVB also occurs though less commonly, in acute anterior MI.

In the GUSTO-I trial, AVB occurred in about 4% of patients with anterior MIs, a rate similar to that seen in previous studies The development of AVB, particularly in anterior MI,

has been shown to confer higher in-hospital and long-term mortality. Atrioventricular block in the setting of inferior MI is also associated with higher in-hospital mortality.

Mortality was 27.9 per cent in patients with block and 9.3 per cent in those without; it was significantly higher in both anterior (47.0 per cent *vs.* 11.8 per cent) and inferior (20.4 per cent *vs* 6.7 per cent) infarction groups.

When age, Infarct size, infarct site and block were analyzed simultaneously as predictors of death, block was a significant independent prognostic factor. The relative risk of death, corrected for age and infarct size, in patients showing block was similar for anterior and inferior infarction.

Analysis of deaths revealed a higher incidence of unheralded death in inferior infarcts associated with high-degree block.

Risk stratification in ST-elevation myocardial infarction is enhanced by combining baseline ST deviation and subsequent ST-segment resolution

The extent of initial injury manifested by ST-segment elevation in acute myocardial infarction (STEMI) correlates directly with ventricular contractility, myocardial infarct size and both short- and long-term mortality.

Schreiber *et al* showed that the extent of absolute baseline ST elevation and ST depression was related to clinical outcomes at 24 hours. (51) Over the past decade during the reperfusion era, resolution of baseline ST elevation has also been recognized as a prognostically relevant measure.

Moreover, unlike conventional angiography, ST resolution appears to be a useful

surrogate indicator of both macro- and micro vascular perfusion and is therefore especially valuable in evaluating the success of myocardial reperfusion therapy (acute STEMI trial ASSENT-3)

STUDY DESIGN AND METHODS

Setting — Coronary Care Unit, Department of Cardiology, Govt General Hospital, Madras Medical College, Chennai-3

Study design — Single centre, non randomized, observational and Prospective study

Patient Selection

All patients admitted between October 2007 and March 2008 with a diagnosis of Acute STEMI in coronary care unit (CCU) of our department were evaluated systematically for inclusion into study using the data which includes demographic, and diagnostic information.

All patients received standard clinical care including monitoring of vital functions in a coronary care unit during the initial hospital stay .All patients were given chewable Aspirin 300 mg, clopidogrel 300 mg. and atorvastatin. Eligible patients were thrombolysed with Streptokinase 1.5 million Units over 1 h.

Inclusion criteria

Patients were included in this study if they fulfilled the following criteria -patients with Acute STEMI- within 7 days of MI

Exclusion criteria

STEMI more than 7 days duration

Preexisting severe co morbid conditions e.g.CKD,Cor Pulmonale which may influence or modify the clinical course and outcome which may also preclude acquisition of adequate echocardiographic and other data.

.NON ST Elevation Myocardial Infarction Patients

Study design

Demographic, clinical, diagnostic, management, and survival data were obtained and recorded. Age and sex distribution, risk factor distribution- Hypertension, diabetes, dyslipidemia, smoking, family history of premature CAD were identified and recorded.

Clinical data

Death was defined as all-cause mortality during hospitalization.

Vital signs and Killip class findings were collected at the time of hospital presentation.

Killip class I was defined as the absence of congestive heart failure,

Class II as the presence of rales and/or jugular venous distention,

Class III as the presence of pulmonary edema, and

Class IV as cardiogenic shock.

Patients with cardiogenic shock were prospectively identified.

Cardiogenic shock was defined as systolic blood pressure <90 mm Hg for 1 h that was

not responsive to fluid administration alone, thought to be secondary to cardiac dysfunction, and associated with signs of hypoperfusion or cardiac index 2.2 liters/min/m2 and pulmonary capillary wedge pressure >18 mm Hg. Patients in whom systolic blood pressure increased to >90 mm Hg within 1 h after administration of positive inotropic agents, or patients who died within 1 h of hypotension but met other criteria for cardiogenic shock, were still classified as having cardiogenic shock.

To characterize the temporal relationship of shock to thrombolytic therapy, the occurrence of shock was also analyzed based on its timing after enrollment: 1 h, >1 to 2 h, >2to 6 h, >6 to 24 h, >24 to 48 h, and >48 h.

Peripheral signs of hypoperfusion included−

Altered sensorium (alteration in mental status or loss of consciousness),

Oliguria (persistence of <30 mL/h urine output), and cold, clammy skin.

Diagnoses of ventricular-septal defect, ventricular rupture, and mitral regurgitation were made on the basis of clinical and echocardiographic evaluation.

Electrocardiographic Data

STEMI was diagnosed based on following ECG Criteria and STEMI was later confirmed by the elevation of cardiac enzymes with CK-MB.

ST-segment elevation of at least 0.1 mV in two or more limb leads;

At least 0.2 mV in two or more contiguous precordial leads

Presumed new left bundle branch block

Right ventricular myocardial infarction was diagnosed

If there was at least 1-mm ST segment elevation in lead V4R to V6R.

Atrial infarction was diagnosed using modified Liu's diagnostic criteria of atrial infarction

PR-segment depression >1.2 mm in leads I, II, III associated with any atrial arrhythmias

Liu's diagnostic criteria of atrial infarction

Major criteria

1. PR-segment elevation > 0.5 mm in leads V5 and V6 with reciprocal PR-segment depression in leads V1 and V2

2. PR-segment elevation > 0.5 mm in lead I with reciprocal depression in leads II and III

3. PR-segment depression > 1.5 mm in precordial leads and 1.2 mm in leads I, II, and III associated with any atrial arrhythmias

Minor criteria

1. Abnormal P waves: M-shaped, W-shaped, irregular, or notched

Standard 12-lead electrocardiograms (ECGs) were collected at baseline and 90 minutes of starting streptokinase treatment, then every 24 hours until discharge. Both ST-segment elevation and resolution were analyzed for documenting successful thrombolysis

Further Electrocardiographic analysis included the following

ST segment depression in non infarct leads

Presence of conduction abnormalities- AV block , various fascicular blocks

Presence of arrythmias-

Brady arrythmias

Tachy arrythmias- SVT,Atrial flutter or fibrillation,

VT, VF, AIVR

Successful reperfusion was defined as > 50% ST resolution, relief of angina and presence of reperfusion arrythmias

Reinfarction was defined as re elevation of CK-MB above the upper limit of normal and increase by at least 50% of the previous value or by the presence of new Q waves in the ECG.

ECHOCARDIOGRAPHY

2D transthoracic ECHO and Tissue Doppler imaging were performed on each patient within 24 hours of admission and repeated before discharge and death or after hemodynamic instability. The echocardiograms were analyzed for qualitative and quantitative assessment. The assessments were performed with Philips En Visor C HD and Aloka Echo Machines.

The qualitative review included a complete evaluation of size and function of each ventricle and all valves in addition to LV regional wall motion assessment.

Regional wall motion was scored by a 16-segment model and each segment was analyzed individually and scored on the basis of its motion and systolic thickening.

A segment which is

Hyperkinetic assigned a score =0,

Normal =1

Mild Hypokinesis =1.5,

Hypokinesis =2

Severe Hypokinesis =2.5

Akinesis(negligible thickening) = 3

Dyskinesis (paradoxicalsystolic motion) =4,

Aneurysmal (diastolic deformation) = 5

Wall motion score index can be derived as a sum of all scores divided by the number of segments visualized. A total score for regional wall motion was calculated as the sum of all segment scores .Then separate scores were calculated for infarct and remote zones.

The severity of mitral regurgitation (MR) was semi-quantitatively graded from color-flow Doppler images in the apical four- and two-chamber views

Color Doppler of MR was graded with a 0 to 4 scale (0=none, 1=mild, 2=moderate, 3=moderate to severe, and 4= severe).

The severity of MR was classified as

Mild (jet area/left atrial area, 20% in the absence of wall jet),

Moderate (jet area /left atrial area 20–40%),

Severe (jet area/left atrial area >40%)

Mitral valve leaflet geometry and morphology were assessed for presence of leaflet prolapse, flail, and incomplete closure.

Quantitative analysis was then performed on echocardiograms of sufficient quality. Measurements included, LV dimensions, LV volume, LV ejection fraction (EF), RV function, extent of LV endocardium involved by wall-motion abnormality.

LVEF was measured by M- MODE, Modified Simpson's method, along with eye – balling

LVEF was stratified as

Normal (LVEF 55%),

Mildly reduced (45–54%),

Moderately reduced (35–44%),

Severely reduced (< 35%)

RV function was assessed by TDI.

In addition mechanical complications such as VSR, Chordal rupture, papillary muscle rupture, free wall rupture were also evaluated.

Diastolic dysfunction, pericardial effusion , LV thrombus , tricuspid regurgitation and pulmonary hypertension were analyzed.

Pulsed Doppler mitral inflow velocities were obtained by placing a 1–2 mm sample volume between the tips of the mitral leaflets in the apical four-chamber view. The Doppler beam was aligned parallel to the direction of flow. The following variables were measured in end expiratory apnea:

Peak early filling velocity (E)

Peak filling velocity at atrial contraction (A velocity)

E/A ratio

Deceleration time of the peak E velocity, defined as the slope from peak E extrapolated to the baseline value

Restrictive mitral inflow patterns were defined as E/A ratio >2 with a E-wave deceleration time < 140 ms.

Doppler analysis of pulmonary venous flow was done from left superior pulmonary vein with sample volume of 2 to 5 mm. systolic (S), diastolic (D), S/ D ratio and Atrial reversal (AR) was done.

Tissue Doppler Imaging

TDI of the mitral annulus was obtained from the apical 4-chamber view. A 1.5-mm sample volume was placed sequentially at the lateral and medial mitral annulus. Analysis was performed for the early (E') and late diastolic velocity (A'): peak velocity (E', A'), and peak systolic velocity s'. These variables were analyzed individually, as the average of the medial and lateral annulus.

All Doppler signals were recorded with at100 mm/s. The average of 3 end-expiratory cycles was used. E/E' Ratio was calculated.

Mitral septal annular systolic(S') velocity cut off value of <7.5 cm/s was taken as LV dysfunction.

Similarly septal tricuspid annular systolic(S') velocity was obtained as measure of RV function and cut off value of < 11.5 cm/s was taken as RV dysfunction

RESULT ANALYSIS

Baseline characteristics and clinical presentation

Over a 6 months period, 655 patients were admitted in our institution with a diagnosis of acute STEMI. Their clinical and demographic characteristics are summarized in [Table 5]

Total number of patients enrolled: 655 Total number of patients in survival group: 574, Total number of patients in mortality group: 81

Table 5. Baseline characteristics of patients

Characteristics		Survival Group n=574 (87.6%)	Mortality Group n=81 (12.3%)	P -value
Age (Mean)		52	61	0.001
Male		440	47	0.001
Female		134	34	0.001
Smoker		198	21	0.126
Non smoker		376	60	0.126
Dyslipidemia		1%	2.6%	0.317
F/H x CAD		12	6	0.157
Hypertension	M	18%	10%	0.341
	F	32%	14%	0.341
Type2 DM	M	17%	28%	0.018
	F	36%	63%	0.018
Prior MI	M	11	12	0.473
	F	5	3	0.473
Prior angina	M	46	7	0.415
	F	15	4	0.415
Prior angioplasty		1	–	–
Previous CABG		–	–	–
Systolic BP (mm Hg)		112(90-240)	92 (80-146)	0.161

Diastolic BP (mm Hg)	84(70-120)	70(60-94)	0.259
Heart Rate	78(54-112)	112(102-136)	0.013

Table 5. Baseline characteristics of patients (contd...)

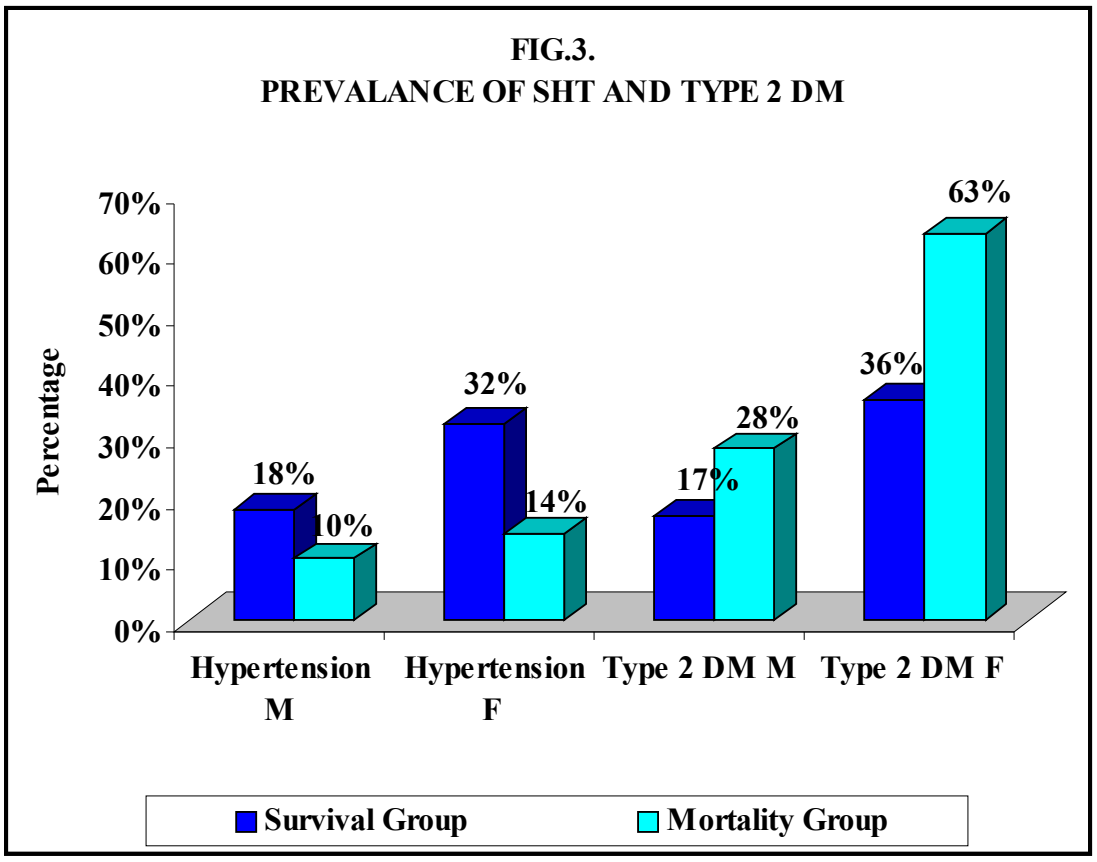
Characteristics	Survival Group n=574 (87.6%)	Mortality Group n=81 (12.3%)	P -value
MI location			
AWMI SK	132	17	0.001
NO SK	193	25	0.001
IWMI SK	79	2	0.100
NO SK	74	–	0.100
IWMI& RVMI SK	18	4	0.113
NO SK	10	7	0.113
IW,RV & PWMI SK	21	14	0.784
NO SK	14	8	0.784
AWMI&IWMI SK	12	3	0.137
NO SK	21	1	0.137
Atrial Infarction	2	1	–
Baseline Killip class			
I	420	26	0.001
II	142	40	0.001
III	12	19	0.001
IV	–	6	0.001
Time to SK(h)	6.5	10.2	0.467
ThrombolyticTherapy	263 (40.1%)	26(32%)	0.001
Prior statin use	72	26	1.0
Prior Aspirin use	72	26	1.0

P value < 0.001 is significant

Most of the patients were males (76.65%) in the survival group but in the mortality group the difference is very narrow (58.02% vs 41.08%) .

The mean age of the patients in the survival and mortality groups are 52and 61 years respectively.

Prevalence of diabetes mellitus and hypertension was higher in females than in male in both groups of patients. The prevalence of diabetes mellitus was higher in the mortality group (63% Vs 28%,). In contrast the prevalence of SHT in mortality group was lower than the survival group (14% Vs 32%).



Patients with previous MI were significantly less (2.8%) in survival group and were significant in mortality group (18.5%).

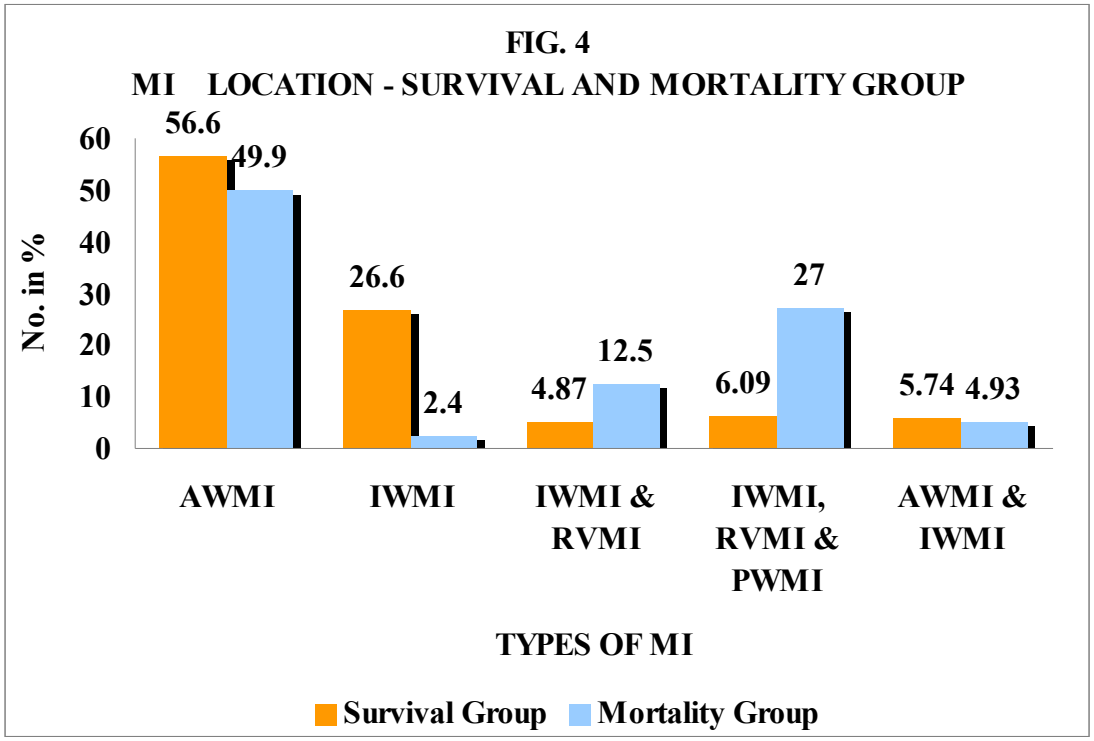
Only one patient in survival group had prior PCI .There was no patients with prior CABG in both groups.

The average baseline blood pressure was lower in the mortality group (92/70 mm Hg) than the survival group (112/84 mm Hg). Also the heart rate on admission was higher in the mortality group (112 Vs 78 bpm).

The most common location of MI was Anterior wall MI in the survival group (56.6%),followed by isolated Inferior wall MI(26.6%), combination of IWMI,RVMI& PWMI(6.07%), AWMI &IWMI (5.74%) and IWMI &RWMI(4.87%).

The most common location of MI was Anterior wall MI in the mortality group(49.9%), followed by combinations of IWMI −IWMI, RVMI & PWMI (27%), IWMI & RVMI (12.5). Death in isolated Inferior wall MI was uncommon (2.4%).

Atrial infarction was present in 3 cases of IWMI, of which 1 patient died.



On admission, majority of patients in the survival group (74.7%) and 32% of the mortality group were in Killip class I. The remaining patients of the mortality group were in higher Killip class – class II 49.3%, class III 23.4%, class IV 7.4%. None of the patients in survival group was in class IV on admission.

The mean time duration between symptom onset and thrombolytic therapy was 6.5 hours in the survival group and 10.2 hours in mortality group.

Only 40.1% of the survival group and 32% 0f mortality group were eligible for thrombolytic therapy.

Significantly more number of patients were on aspirin and statin therapy in the mortality group (12.5%) than the survival group (32.1%).

Baseline characteristics and clinical presentation of patients with cardiogenic shock

Table 6. Demographic and clinical variables (for patients with cardiogenic shock)

Characteristic	Survival Group (n=5)	Mortality Group (n=37)	P -value
Age (mean)	58	63	0.001
Male	2	23	0.001
Female	3	14	0.001
SHT	1	4	0.179
Diabetes mellitus	1	25	0.001
Altered sensorium	–	28	0.001
Oliguria	1	37	0.001
Baseline SBP	104	88	0.248
Baseline HR	94	108	0.324
Baseline Killip class			
I	3	4	0.001
II	2	11	0.001
III	–	17	0.001
IV	–	5	0.001
MI location			
Anterior(AWMI)	2	19	0.001
Inferior(IWMI)	–	–	–
Inferior & RVMI	1	7	0.034
IW, RV & PWMI	2	7	0.095
AWMI& IWMI	–	4	0.001
Atrial Infarction	–	1	0.001
VT/VF	–	5	0.001
AF	–	1	0.001
CHB -TPI done	–	9	0.001
CHB -not done	–	–	–
Time to thrombolysis (h)	6.4	10.8	0.225
Thrombolytic Therapy	2	12	0.008
VSR	1	7	0.001
MR (Mod to Sev)	1	8	0.001

P value < 0.001 is significant

The incidence of cardiogenic shock was 6.4%(n=42),of which only 11.9% survived (n=5) and 88.1% died (n=37) [Table 6]

The mean age of patients in the cardiogenic shock group were higher (63 Vs 58 years).

The baseline mean systolic blood pressure was lower in the mortality group (88 Vs 104 mm Hg).

All patients in the mortality group had tachycardia on admission(average HR= 108 bpm)

16.2% (n=6) of the cardiogenic shock group patients were in Killip class IV on admission. None of the patients in the survival group had cardiogenic shock on admission.

About half of the patients (51.3%) in the mortality group had AWMI. Incidence of combinations of IWMI – IWMI/RVMI & IWMI/RVMI/PWMI were equal (18.9%).

No patients with the isolated IWMI developed cardiogenic shock.

In the mortality group, 5 Patients (13.5%) developed VT/VF.

About one –fourth (24.3%) of the patients in the mortality group developed CHB and none in the survival group.

One third of the patients in the mortality group received thrombolytic therapy. The mean time duration for thrombolytic therapy was higher (10.8 hours) in mortality group (6.4 hours in the survival group).

Cardiogenic shock due to mechanical compilations was higher in the mortality group. Seven patients (18.9%) developed VSR and 8 patients developed MR (21.6%).

Electrocardiographic characteristics

Out of 655 patients, 289 received thrombolytic therapy (44.1 %) among which 263 patients (88.8%) survived and 21 patients (11.2%) died. Thrombolytic therapy was successful (>50% ST resolution) in 106 patients (38.1%). Significant number of patients who had successful thrombolysis survived (95.4%). Few deaths (4.6 %) occurred after successful thrombolysis. The mortality in the failed thrombolysis patients was higher (11.2%) [Table 7]

Significant ST depression in non -infarct zone was found in 47 .4% of the mortality group and 34.8% of the survival group.

Mobitz type I second degree block was present in 1.7% of the survival group. But the incidence of type II second degree AV block was higher in the mortality group (4.3%) than the survival group (0.34%).

New onset LBBB was twice common in the mortality group (2.4% Vs 1%)

Table 7 Electrocardiographic variables

Characteristic		Survival Group	Mortality Group	P -value
ST Resolution (Thrombolytic Therapy)	<50%	158	21	0.038
	>50%	105	5	0.001
ST depression		34.8%	47.4%	0.001
VT/VF		8	12	0.371
AF		2	1	0.564
II degree AVB-	Type I	10	–	0.001
	Type II	2	4	0.414
LBBB		6	2	0.157
RBBB		48	12	0.001
RBBB&LAFB		17	7	0.041
RBBB& LPFB		1	3	0.001

P value < 0.001 is significant

The incidence of RBBB and fascicular blocks was higher in the mortality group-

RBBB 14.8% Vs 8.3%

RBBB &LAFB 8.6% Vs 2.9%

RBBB&LPFB 3.7% Vs 1%

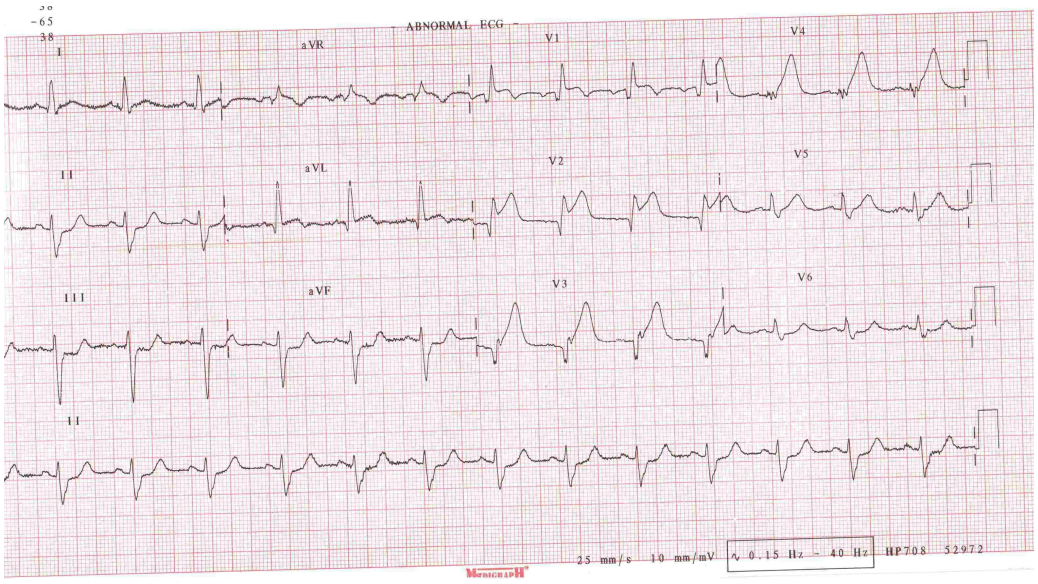


Figure 5 ECG of a patient showing AWMI with RBBB and LAFB

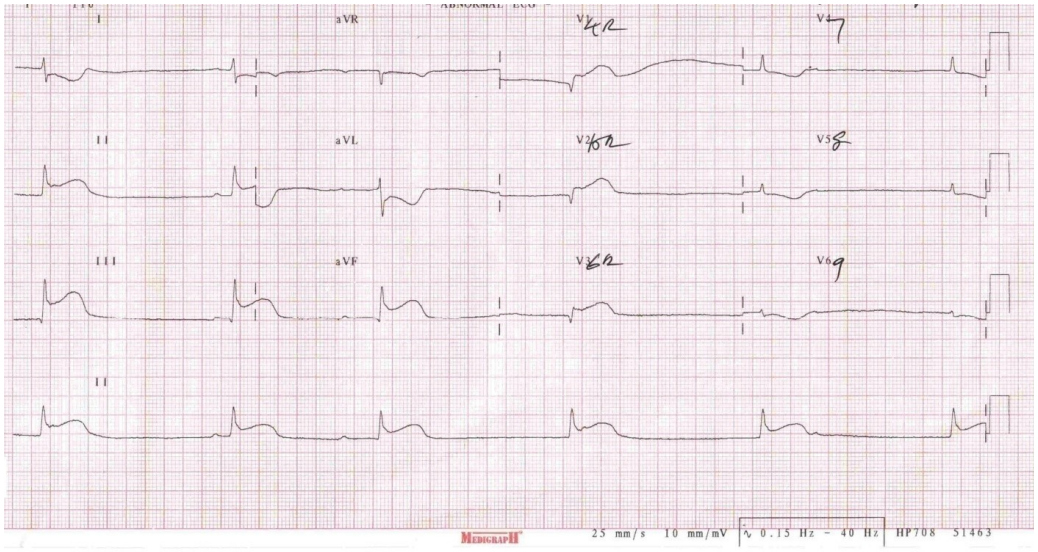


Figure 6 ECG showing Acute IWMI & RVMI. The rhythm is AV dissociation with III degree AV block

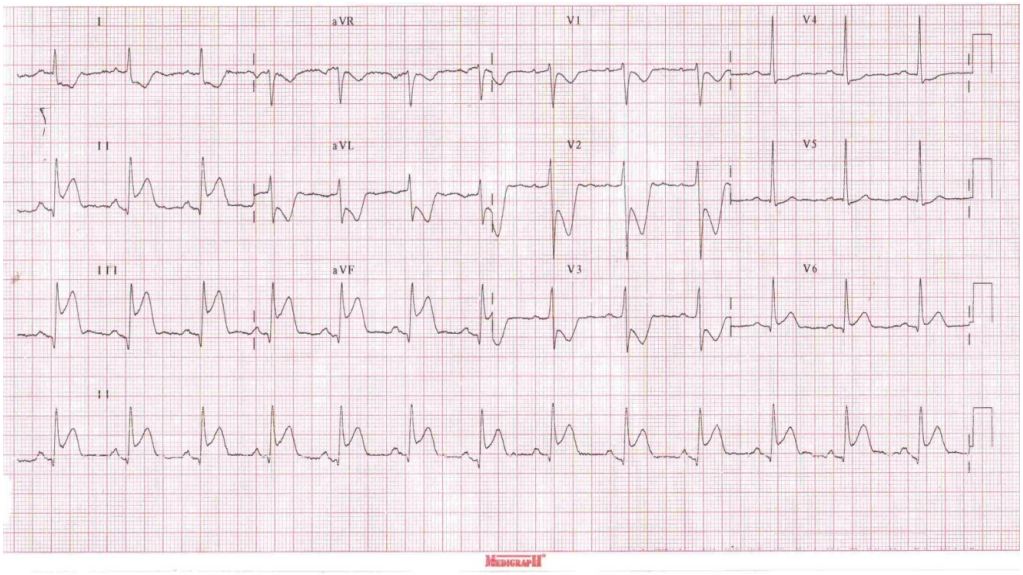


Figure 7 ECG of a patient with Acute IWMI with non infarct zone ST depression in precordial leads

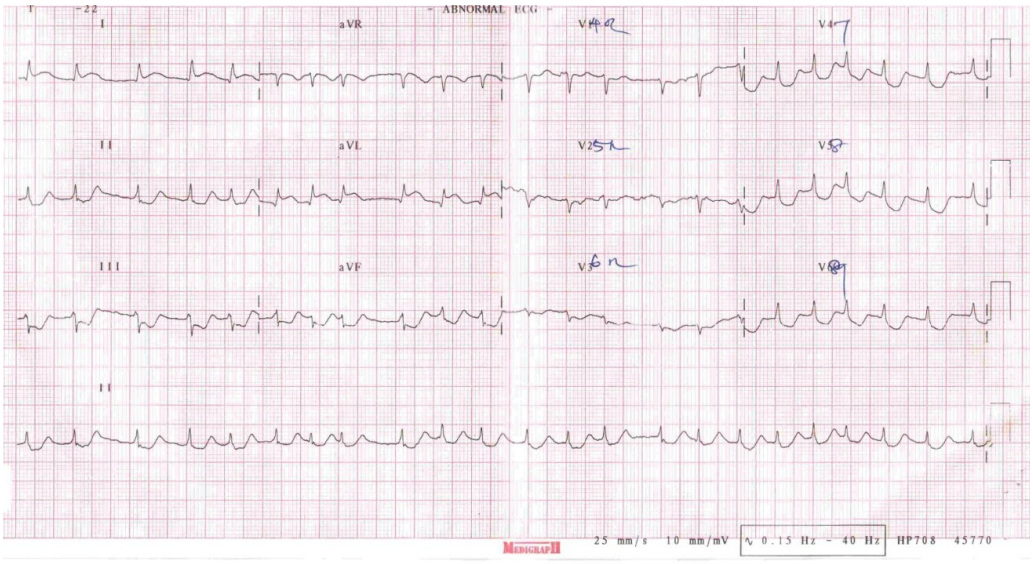
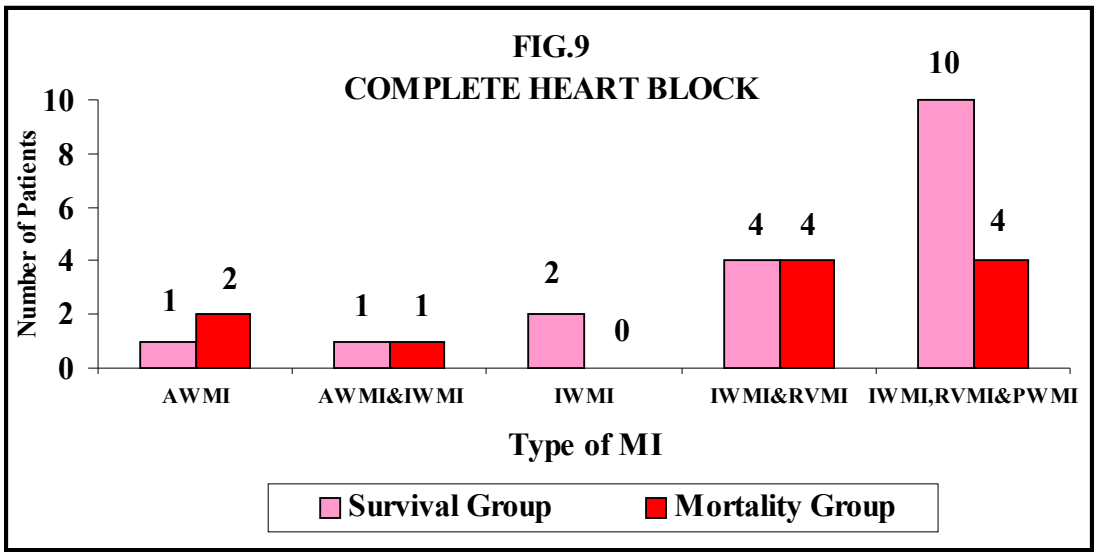


Figure 8 ECG showing STEMI with Atrial fibrillation

Table 8. Electrocardiographic variables-Complete Heart Block

MI location	Survival group (n =18)		Mortality group n=11	
	M (n =11)	F (n=7)	M (n=3)	F (n=7)
AWMI	–	1	1	1
AWMI&IWMI	–	1	–	1
IWMI	1	1	–	–
IWMI&RVMI	3	1	1	3
IWMI,RVMI&PWMI	7	3	1	3

Complete heart block (CHB) developed in 29 patients and all of whom required temporary pacemaker (survival group 3.1% (n= 18); mortality group 13.5% (n=11)[Table8]. CHB was common in combinations of IWMI than in isolated IWMI or AWMI and associated with increased mortality and was three times more common in the mortality group .



Echocardiographic analysis

Table .9 Echocardiographic variables - M-Mode

M-Mode	Survival group	Mortality group
LVEDD(cm)	5.2±0.6	5.8±0.5
LVESD(cm)	3.8±0.8	4.9±0.4
LVEF (%)	48.3±7.8	39.2±9.6
LVH (%)	18	11%

The LV dimensions and volume were higher in the mortality group. [Table 9 and 10] LVEDD 5.8±0.5 Vs 5.2±0.6 cm/ LVESD 4.9±0.4 Vs 3.8±0.8cm.

The EDV and ESV values were increased proportionately. LVEDV 123±46 Vs 112±39 ml; LVESV 87±35 Vs 82±36 ml. The mean LVEF was 30.4±12.1 in the mortality group and 46.2±8.2 in the survival group (using modified Simpson's method).

Mean LV ejection fraction was higher in the survival group (EF 48.3±7.8% Vs 33.9±9.6%) by Teicholtz method also.

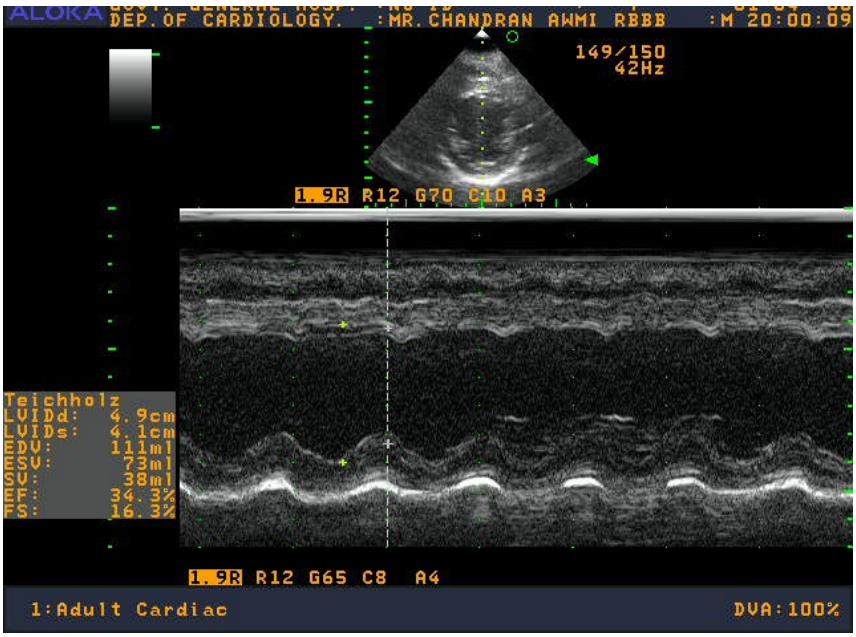


Figure10 M-Mode Echo- of a patient with AWMI showing hypokinesis of IVS with compensatory hyperkinesis of LVPW

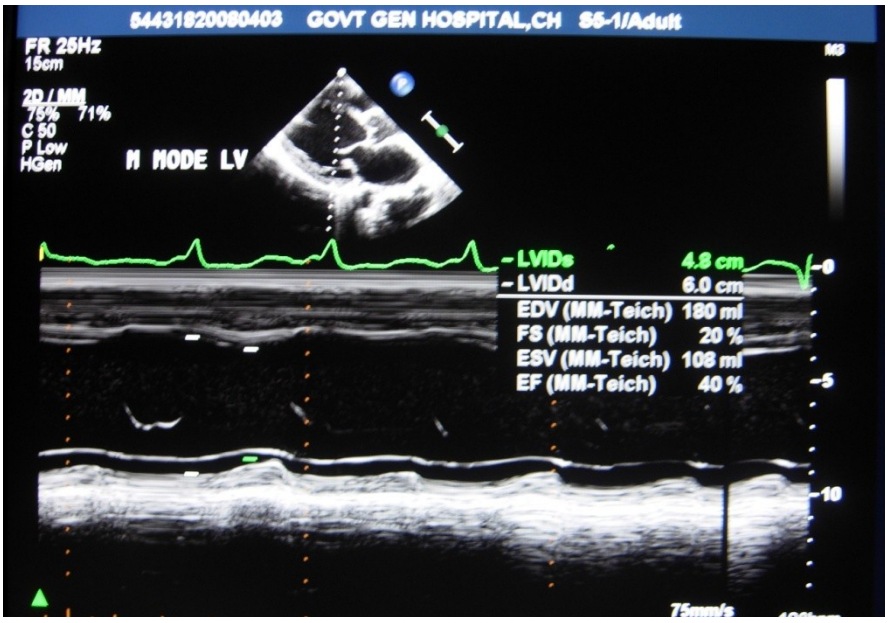


Figure 11 M-Mode Echo- of a patient with AWMI showing Akinesia of IVS and absence of hyperkinesis of LVPW

Table 10.Echocardiographic variables -2D Echo

2D Echo	Survival group	Mortality group	P value
LVEDV (ml)	112±39	123±46	0.08
LVESV(ml)	82±36	87±35	0.014
EF (modified Simpson's)	46.2±8.2	30.4±7.1	0.0004
WMSI global	1.4±0.4	2.2±0.5	0.0001
Infarct zone	1.8±0.3	2.6±0.3	0.0001
Non infarct zone	0.9±0.3	1.2±0.3	0.0001
Pericardial effusion >5mm	1%	3%	–
LV thrombus	1%	8%	0.004
MR Grade Mild	57(10%)	20(24.6%)	0.034
Mod to Sev	28 (4.8%)	25 (30.8%)	0.09
VSR	1	7	0.001

P value < 0.001 is significant

The Wall Motion Score Index (global, infarct zone & non infarct zone) was higher in the mortality group .All grades of mitral regurgitation (MR) was more common in the mortality group. The incidence of significant MR (moderate to severe >2+ was much higher (30.8%) than the survival group (4.8%).

There was no significant difference in mild MR between the two groups (12.3%Vs 10%).

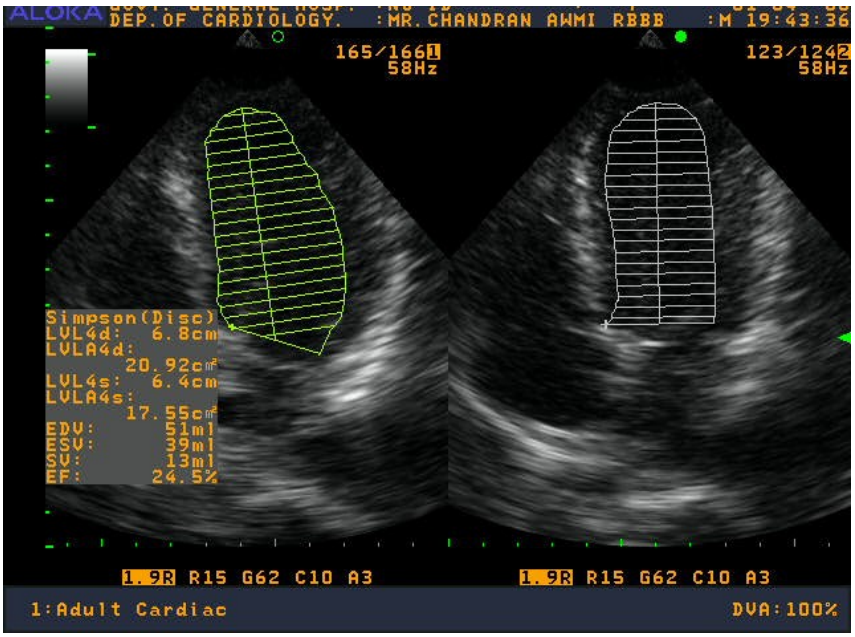


Figure 12 2D echo–apical 4 chamber view. LVEF assessment by modified Simpson's method.

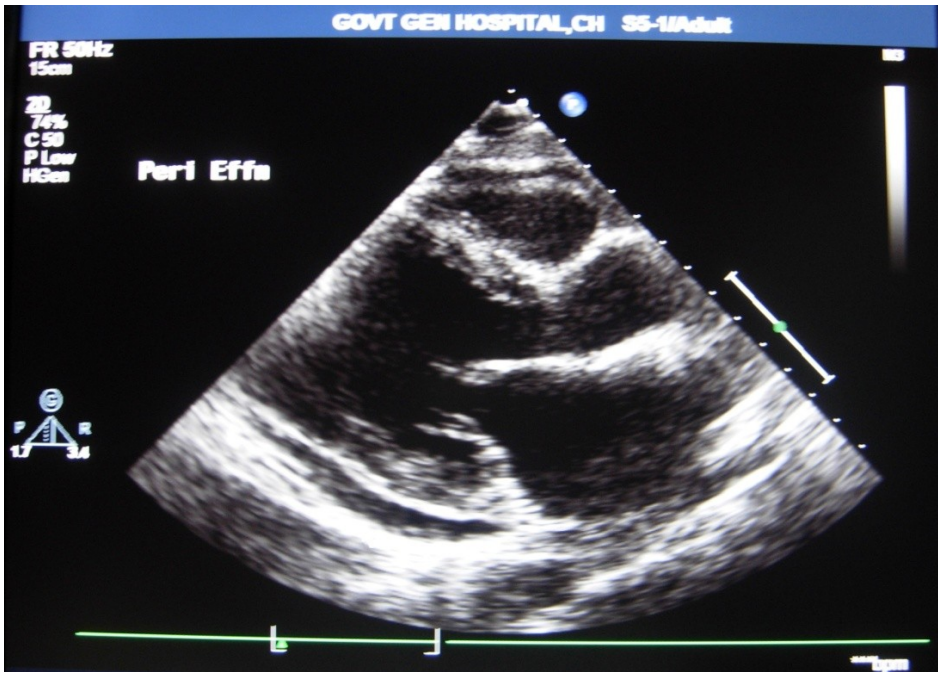


Figure 13 2D Echo (PLAX view) – dilated LA and LV with mild Pericardial effusion

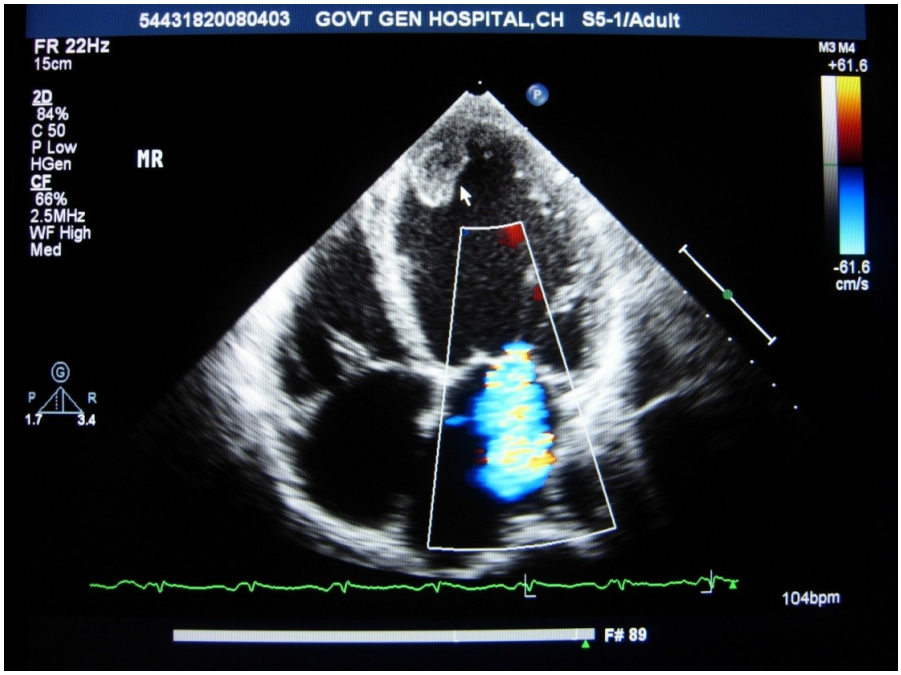


Figure 14 2D Echo (apical 4 chamber view) demonstrating Mitral Regurgitation (mod MR 2+). Thrombus is seen in the LV apex (arrow)

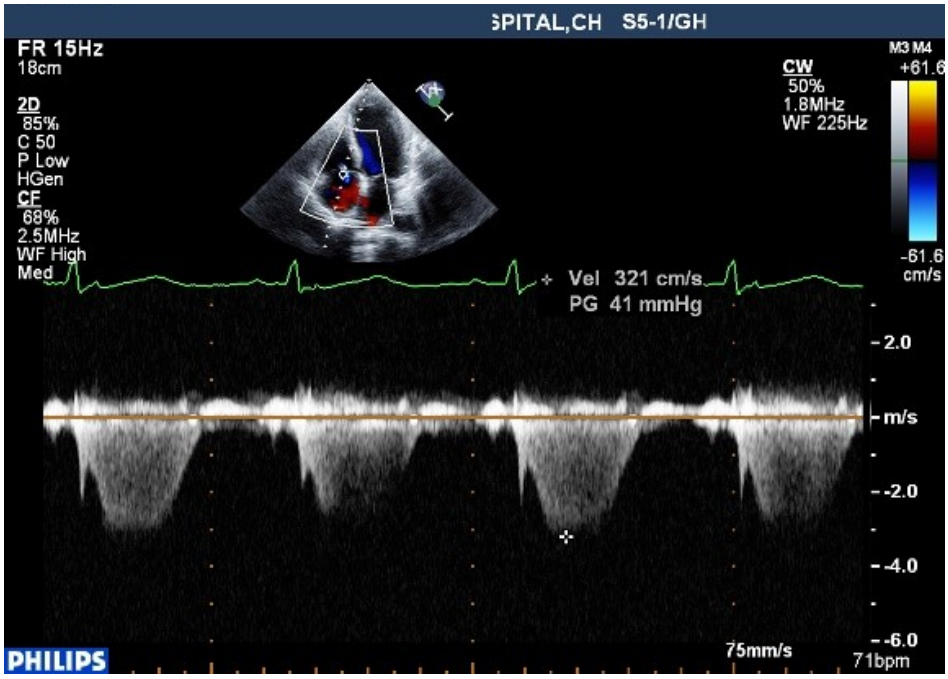


Figure 15 Tricuspid inflow continuous wave doppler. The TR velocity is 3.2 m/s. patient is had mild PAH

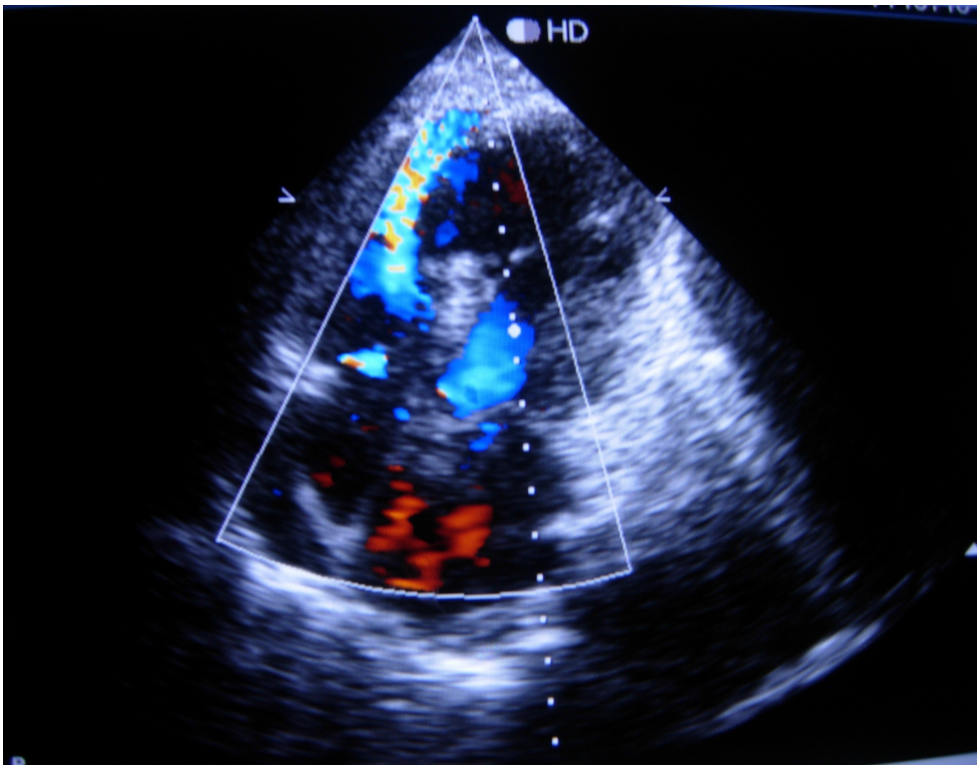


Figure 16 Echocardiography showing Apical VSR in a patient with AWMI

Table 11 Echocardiographic variables –Doppler study

Characteristic	Survival group (n=574)	Mortality group (n=81)	P-value
Mitral inflow (cm/s) E	89±16	103±29	0.07
A	59±12	40±14	–
E/A	1.26	2.19	0.001
DT >140ms	533 (93%)	50(62%)	0.007
DT<140 ms	41(7%)	31(38%)	0.007
PV Doppler S/D ratio >1	528 (92%)	13 (15%)	0.9
S/D ratio <1	46(8%)	68 (85%)	0.001
TDI (cm/s)			
Mitral annulus (cm/s)- E’	10.8±1.1	4.6±1.1	0.005
S’	7.1± 1.4	5.6±1.2	0.001
Tricuspid annulus S’ (RVMI) <11.5	17%	33%	0.005
E/E’ RATIO >15	8.24±1.1	22.3±3.2	0.0001

P value < 0.001 is significant

The Doppler Echo indices showed significant difference between the two groups.[Table 11]. Mitral inflow E/A ratio ≥2 .0 was present in 91.3% (n=74)of the mortality group.

Majority of patients in the survival group (93%) had Mitral deceleration time (DT) of >140 ms where as DT of < 140 ms was associated with increased mortality (38% Vs 7%).

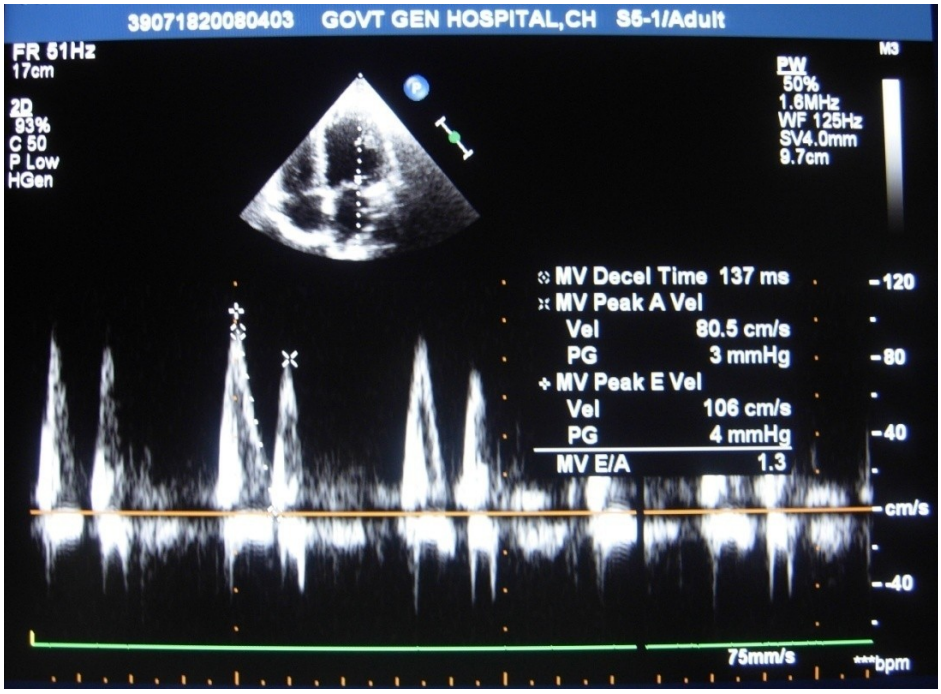


Figure 17 Pulsed wave Doppler echo of mitral inflow showing shortened DT (<140ms) in a patient with AWMI

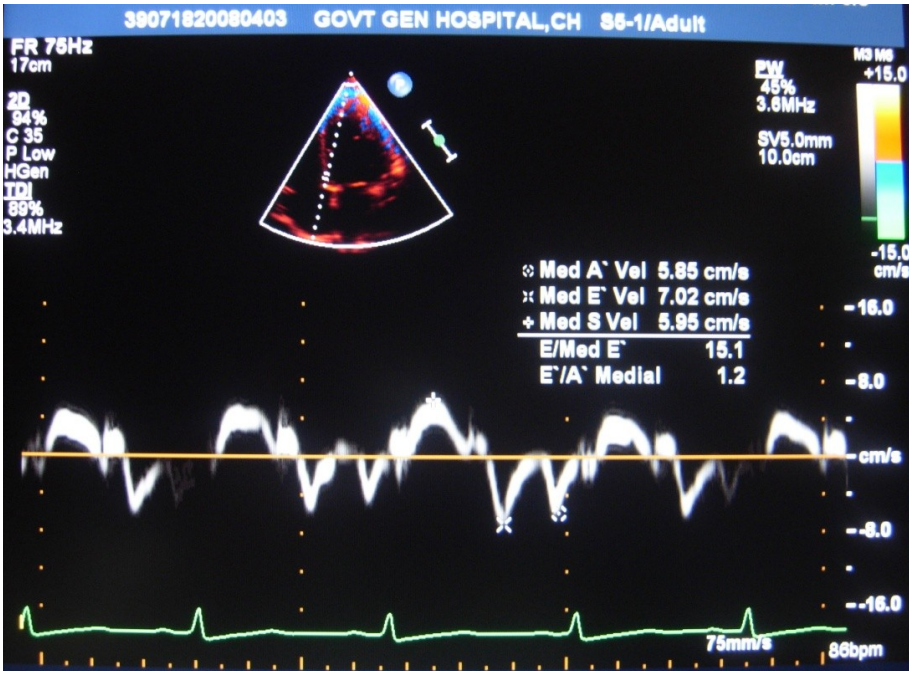


Figure 18 TDI of the same patient as in figure 17 showing raised E/E' ratio of > 15 .The S' value is 5.95 suggesting LV dysfunction.

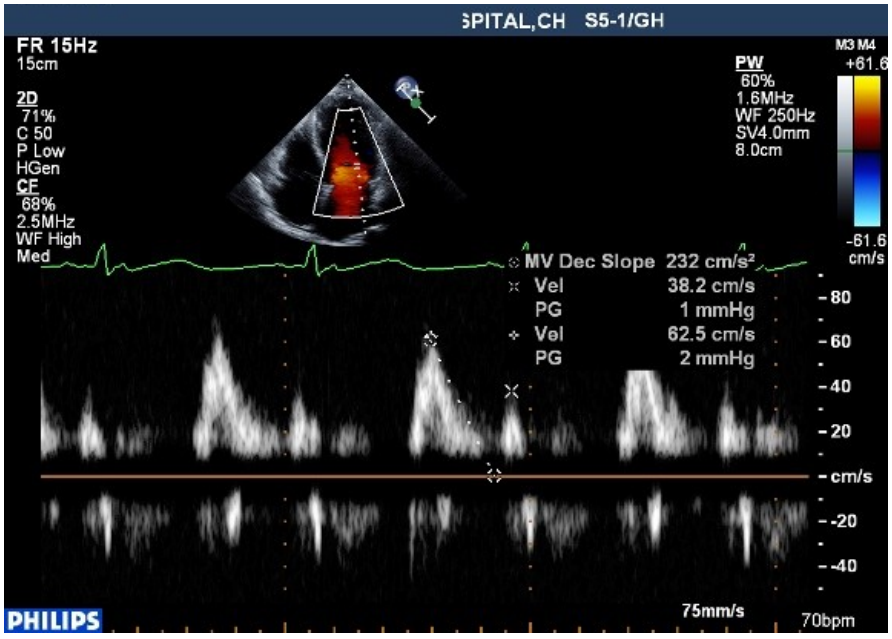


Figure 19 Pulsed wave Doppler echo of mitral inflow in a patient with AWMI

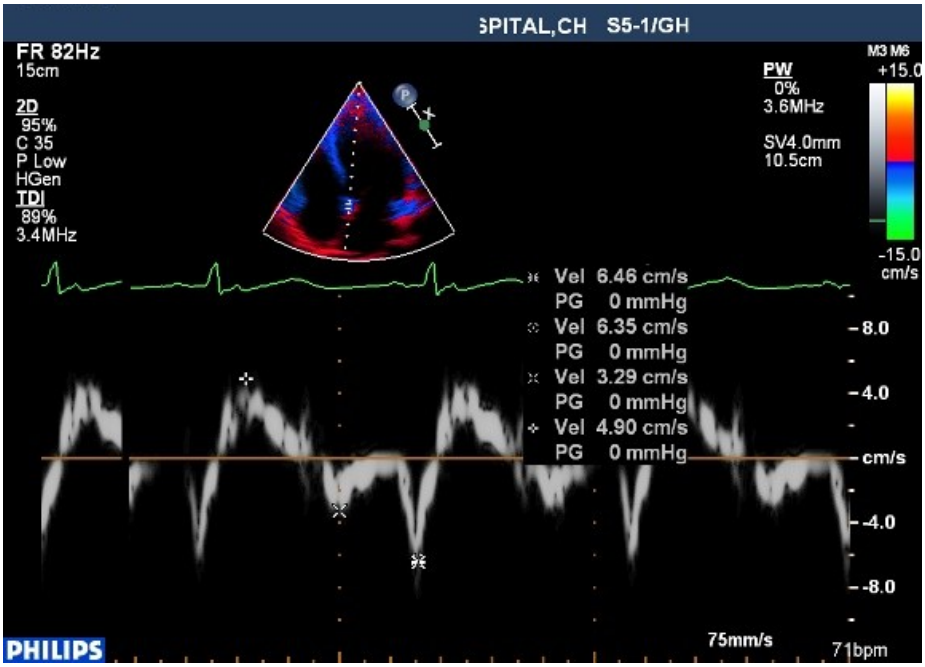


Figure 20 TDI of the same patient as in figure 19 showing reduced E' value with raised E/E' ratio of > 15 .The S' value is 4.90 suggesting LV dysfunction.

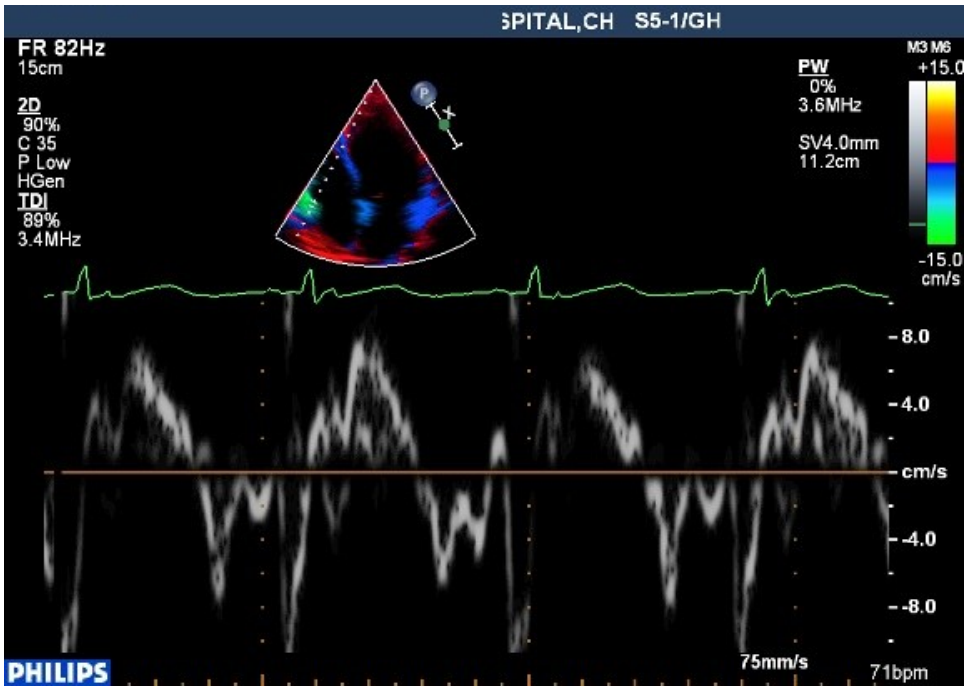


Figure 21 Tricuspid annular TDI in a patient with IWMI and RVMI .The S' value is <11.5 cm/s suggestive of RV dysfunction

S/D ratio of pulmonary venous flow > 1.0 was associated with higher survival rate

(92%) but value of <1.0 was associated with higher mortality (85%).

The mitral annular Systolic (S') and early diastolic (E') velocities were well below the normal range in the mortality group. The average E' velocity was 4.6±1.1 (Vs survival group10.8±1.1 cm/s).

Mitral E/E' value of >15 was uncommon in the survival group (8%) and high in the mortality group (78%).The mean E/E' ratio in the mortality group was 22.3 ±3.2.

One-third of RVMI patients died (33% Vs 17%) who had a Tricuspid annular systolic velocity (S') of < 11.5 cm/s which is suggestive of RV dysfunction.

Baseline hyperglycemia was more common in the mortality group of patients.

Echocardiographic data analysis in patients with cardiogenic shock [Table 12**]**

The mean LV EDV and LVESV were higher in the patients who died of cardiogenic shock than in those died of causes other than cardiogenic shock. Also LVEF was significantly lower in that group of patients.

The presence of non infarct zone hypokinesis was associated with higher mortality (78.3% Vs 20%).

42% of the cardiogenic shock in the mortality group had RV dysfunction.

Significant MR was present in 46.2% of patients who died of cardiogenic shock and none had Significant MR who survived of cardiogenic shock.

Seven out of eight patients with VSR died (87.5%).

Restrictive mitral inflow pattern and mitral E/E' ratio >15 was more frequent in the mortality group.

LV thrombus and pericardial effusion was notably absent in patients who survived cardiogenic shock.

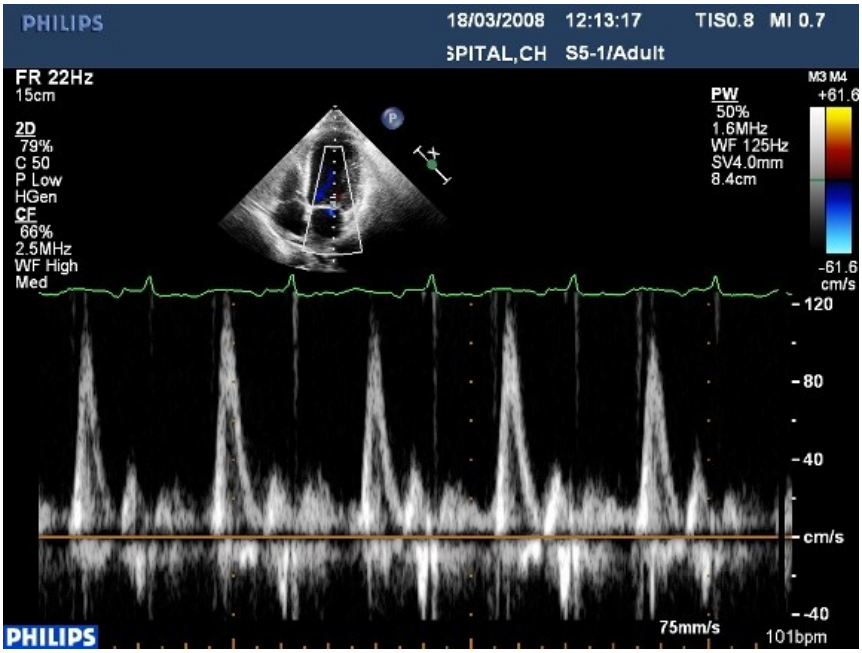


Figure 22 Pulsed wave Doppler echo of mitral inflow showing restrictive filling pattern in a patient with AWMI who developed Cardiogenic Shock

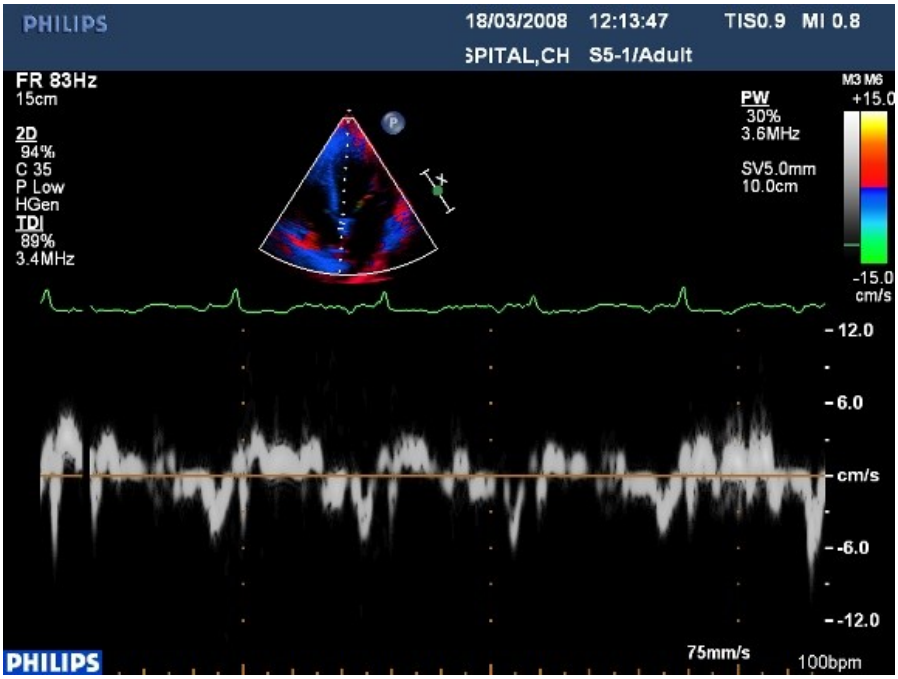


Figure 23 TDI of the same patient who developed cardiogenic shock as in figure 22 showing markedly reduced E' (<3 cm/s) with raised E/E' ratio of > 15. The S' value is

also reduced

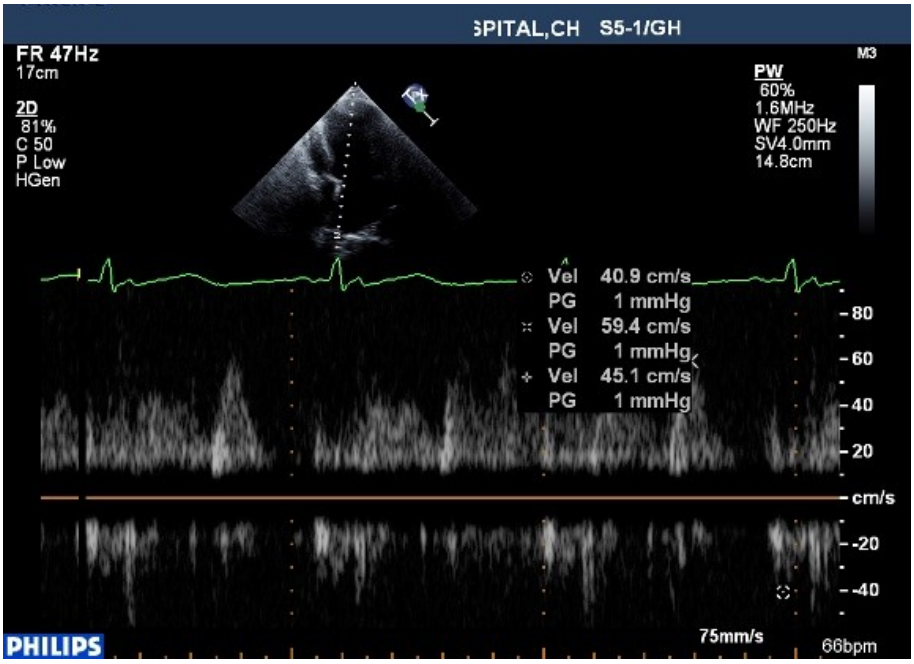


Figure 24 Pulmonary venous flow Doppler in a patient with AWMI showing S < D. Atrial reversal velocity is increased

T able 12 .Echocardiographic profile in cardiogenic shock

Characteristic	Survived (n=5)	Died (n =37)	P- value
LVEDV (ml)	114±26	126±34	0.001
LVESV(ml)	88±39	92±36	0.004
LVEF%	34±8.2	30.4 ±12	0.016
Non infarct zone hypokinesis	1	29	0.001
RV dysfunction	–	42%	0.001
MR Mild (<2+)	1	–	0.064
Mod- Sev (≥2+)	–	46.2%	0.001
VSR	1	7	0.001
Mitral DT <140 ms	3	31	0.001
DT > 140ms	2	6	0.073
E/A >2	3	31	0.001
E/E' ratio >15	3	29	0.0001
LV thrombus(n=3)	0	3	0.094
PEF > 5 mm	0	12	0.001

P value < 0.001 is significant

Table 13 .Biochemical profile

	Survival group (n=574)	Mortality group (n=81)
Random Blood Sugar (mg%)	112±24	194±34
Blood Urea(mg%)	24±11	36±17
Serum Creatinine(mg%)	0.7±o.4	1.1±o.5
Total Cholesterol (mg%)	170±34	194±29
HDL(mg%)	38±6	34±5
TGL(mg%)	226±18	272±24

In- hospital events and mortality

In-hospital complications were high in the mortality group.[Table14] Of the cardiac events, Asystole, occurred only in the mortality group (9.8% n=8). Other major cardiac events were cardiogenic shock (45.6% Vs 0.8%), VT/VF (14.8%Vs1.4%), CHB (13.5% Vs 2.9%), pulmonary edema (9.8% Vs 1.0%), VSR (8.6%), Reinfarction (3.7% Vs 1%) and pericarditis (7.4% Vs 2%).

The major non cardiac events were CVA (3.7% n=3) and acute renal failure (1.2% Vs 0.6%).

Table 14 .In- Hospital complications

	Survival group (n=574)	**Mortality group (n=81)**	**P value**
VT/VF	8	12	0.06
AF	3	1	0.042
CHB	17	11	0.001
Asystole	–	8	0.0001
VSR	1	7	0.001
Reinfarction	6	3	0.072
Pericarditis	12	6	0.086
Pulmonary edema	6	8	0.052
Cardiogenic shock	5	37	0.0001
Acute Renal Failure	4	1	–
CVA	–	3	0.001

P value < 0.001 is significant

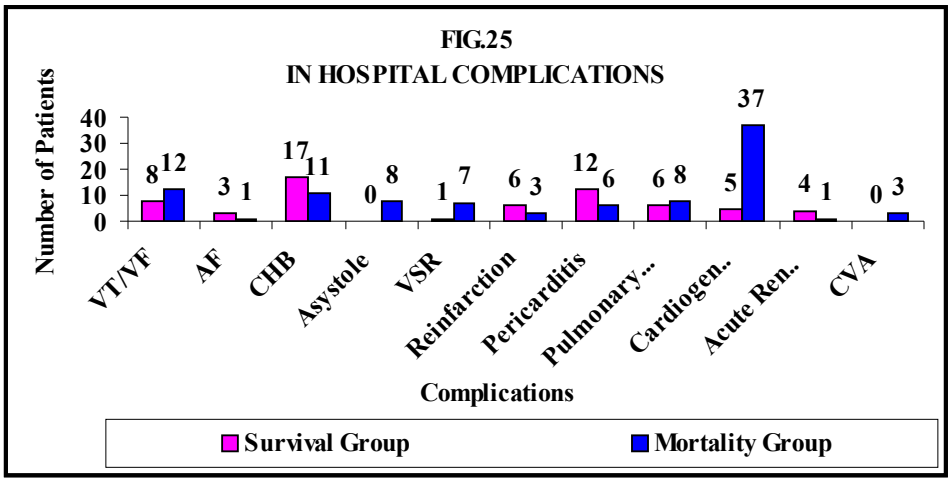


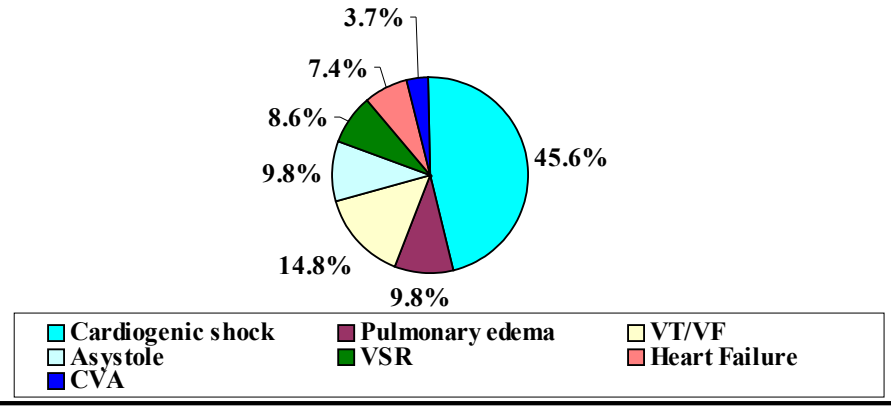
Table 15. In- Hospital mortality –causes

Causes	Number of patients (n=81)	%
Cardiogenic shock	37	45.6
Pulmonary edema	8	9.8
VT/VF	12	14.8
Asystole	8	9.8
VSR	7	8.6
Heart Failure	6	7.4
CVA	3	3.7

Most common cause of death was cardiogenic shock (45.6%) [Table 15]followed by ventricular arrhythmias (VT/VF 14.8%), pulmonary edema (9.8%), VSR (8.6%), CHF (7.4%) and CVA (3.7%).

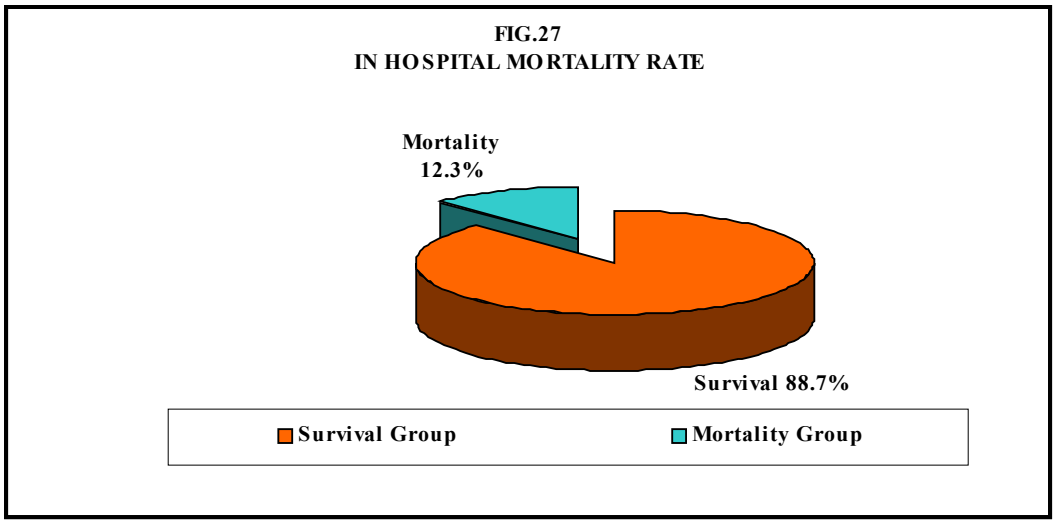
FIG. 26

IN HOSPITAL MORTALITY



DISCUSSION

In this study, mortality rate during hospitalization with acute STEMI was 12.3%. Though this is considerably higher than what has been reported from previous randomized clinical trials. This discrepancy is due to selective bias in the inclusion criteria of the randomized clinical trials which selectively excluded certain high risk group of patients such as elderly.



In the randomized trials on fibrinolysis for STEMI, the reported mortality ranged from 4% to 7%. As per CREATE registry data from India, mortality rate was 7.9% at tertiary care centers for acute coronary syndrome which included both, patients with unstable angina and AMI.

However, in non-randomized trials, especially in the registry data, the reported mortality is usually higher. In a study published in Scotland, the case fatality following AMI was 22.2% in a group of 11,778 patients. In the MITRA and MIR registries data from Germany, the overall mortality was 15%.

The higher mortality observed in our patients can have several reasons. Firstly, most of

our patients received only thrombolytic therapy and primary percutanous coronary angioplasty was not done.

Secondly, our hospital being a tertiary care center, there could be a referral bias in the enrolment of patients. Patients who are sicker may be referred from primary and secondary level hospitals to our institution. However, this higher mortality compared well with the observational data from the West.

Gender and age:

Males predominated females by 3: 1 ratio in the incidence of STEMI (74.3% Vs 25.6%).

Women had higher prevalence of hypertension, diabetes mellitus and higher in-hospital mortality than men (25.6% v. 9.6%, $p<0.001$). The demographic characteristics and mortality rate in females in this study match the report from Trappolini et al. In their study, the overall mortality rate during hospitalization was 24.4% for women and 13.2% for men; women were significantly older than men, had higher prevalence of hypertension and diabetes mellitus, and thrombolytic therapy was prescribed less often in them. In the MONICA project also diabetes mellitus was more common in women and they had higher in-hospital mortality (21.2% v. 12.7%).

Diabetic females had higher mortality rate (30%) than diabetic males (14.7%) The in-hospital mortality in patients above 75 years of age was 33.4%. In the study by Ruiz-Bailen et al. the mortality was 17.7% in patients between age of 75-84 years and 25.8% in patients more than 84 years of age.

Family history of premature CAD and dyslipidemia were not associated with significantly higher mortality (p value 0.157 and 0.317). Prior MI carried poor outcome. This

could be due to the fact that older patients or those with prior infarction may have an inadequate compensatory hyper kinesis response of the uninvolved myocardium.

The most common MI location was anterior wall MI in the survival and mortality group .Although isolated IWMI was the next common group, death occurred only in two patients (2.4%).

Patients with inferior MI who also had RV myocardial involvement were associated with increased risk of death, shock and arrhythmias. This increased risk is related to the presence of RV myocardial involvement itself rather than the extent of LV myocardial damage.

An analysis from the Collaborative Organization for RheothRx Evaluation (CORE) trial showed lower proportion of males with RV myocardial involvement (72.4%) than those without RV myocardial involvement (80.4%) or anterior MI (79.1%) ($p = 0.001$).

There was also a significant difference in the distribution of Killip class among the three groups, with a greater proportion of patients with anterior MI and RV myocardial involvement in Killip class 3 and 4 than patients without RV myocardial involvement.

Patients with RV myocardial involvement had significantly lower systolic blood pressure (123 mm Hg) compared with patients without RV myocardial involvement (129.9 mm Hg) or anterior MI (134.4 mm Hg) ($p = 0.001$).

In this study, combinations of IWMI had higher mortality rate. Involvement of RV myocardium carried poor prognosis and death occurred in one- third (33%) of RVMI cases. This is in contrast to the previous beliefs that IWMI is relatively innocuous with favorable outcome than AWMI. This group of patients had higher rate of in hospital complications – complete heart block. , hypotension and cardiogenic shock. The mortality was high which is

independent of LV ejection fraction.

The electrocardiographic findings of ST segment depression in non infarct leads was associated with increased mortality ($p<0.001$).

Conduction abnormalities such as high grade AVblock, LBBB, and bifascicular blocks were more frequently associated with death. RBBB & LAFB was three times more common in the mortality group (8.6% Vs 2.9%). RBBB with LPFB was rare and three out of the four patients died ($p <0.001$).

Echocardiographic predictors of in –hospital mortality and cardiogenic shock

Echocardiographic markers of regional function were associated with LVEF. A substudy of SHOCK trial by Michael H. Picard et al, showed variables that were positively correlated with LVEF were number of myocardial segments in the remote zone and wall-motion score of this zone.

Variables that were negatively correlated with LVEF included end-diastolic volume, end-systolic volume, total wall-motion score, total wall-motion score index, infarct zone wall-motion score, and number of infarcted segments, sphericity index, and the extent of dysfunction.

Severity of MR appeared related to factors that influenced mitral leaflet closure geometry and the presence of the incomplete mitral leaflet closure pattern.

The significant echocardiographic predictors of in – hospital mortality were LVEF and severity of MR.

Several studies have demonstrated the prognostic importance of clinical and biological

data in the risk stratification of patients with acute coronary syndrome (ACS). Clinical evidence of heart failure is a powerful predictor of worse prognosis in these patients.

However, elevated LV filling pressure may be clinically silent. Besides its usefulness for quantification of LV systolic function, Doppler echocardiography provides useful information regarding LV filling pressure.

Ommen et al. have previously reported that ratio of early transmitral flow (E) to early mitral annulus velocities (E') 15 indicates elevated LV end diastolic pressure measured by cardiac catheterization and associated with poor prognosis.

Other investigators have observed a poor outcome in a retrospective cohort of patients with ACS when E/ E' ratio >15.

The present data indicate that

(i) bedside Doppler echocardiography obtained on admission provides prognostic information in patients with ACS and

(ii) the association between E/E' ratio >15 and high mortality and morbidity was independent of clinical evidence of heart failure, as well as of renal dysfunction, blood glucose level, LV systolic dysfunction and MR.

Worsening diastolic function is associated with rising left atrial pressures. This results in a higher early diastolic gradient across the mitral valve, with rapid equalization of the pressures in the left atrium and ventricle. Initially, this normalizes the DT and mitral E/A ratio (pseudonormalization), but ultimately the mitral E wave becomes markedly predominant and the DT becomes very abbreviated.

Advanced diastolic dysfunction is associated with an adverse outcome after acute MI, with an abbreviated DT being particularly predictive of poor outcome.

The analysis of mitral inflow using pulsed Doppler signal recorded at the tips of the leaflets has a prognostic value in various cardiac diseases. Higher mitral E/A ratios and shorter deceleration times that define the restrictive pattern indicate an increased risk of adverse events after myocardial infarction.

Similarly Temporelli et al. have also observed a poor outcome in 571 patients enrolled in the GISSI-3 trial when mitral deceleration time is shortened.

The E/E' ratio has been well validated to assess LV filling pressures. The threshold of E/ E' 15 identifies at best patients with mean LV diastolic pressures above 12 mmHg measured by micromanometer-tipped catheters.

Raised LV filling pressures indicate a relatively load intolerant myocardium. This may result from major myocardial damage due to coronary occlusion or conversely from minor damage associated with a previous stiff LV chamber due to aging, hypertension, diabetes, or coronary atherosclerosis.

These patients with increased LV filling pressures show poor outcome in this study with three times increased risk of in hospital mortality.($p<0.001$)

In addition, the direct recording of mitral annulus motion using tissue Doppler is easily obtained. The E/ E' ratio gives a reasonable estimate of LV filling pressures and remains valid in the presence of sinus tachycardia, functional MR, and preserved or depressed LV systolic function.

The principal finding of the this study - the E/E' ratio >15 is a powerful predictor of higher in- hospital mortality after acute MI.

An E/E' ratio of >15 proved to be superior, in this respect, to other clinical or echocardiographic features measured in this study. Furthermore, it provided prognostic information incremental to these parameters.

Elevated PCWP is associated with a higher mortality rate after acute MI. There are several potential explanations for this. Higher LV filling pressures are usually indicative of larger infarcts with more severe systolic dysfunction .In addition, LV pressure overload predisposes to ventricular remodeling, neurohormonal activation, and increased excitability all of which would be expected to adversely affect the outcome.

Despite its prognostic value, the measurement of PCWP has obvious drawbacks. In contrast, Doppler echocardiographic assessment of transmitral flow provides a noninvasive means of identifying patients with elevated left atrial pressures.

The current data confirm the prognostic value of a short DT. In addition, they corroborate the well-documented prognostic value of clinical indicators of LV filling pressures, such as Killip class.

This study demonstrates that, in the acute setting, elevated E/E' correlates well with traditional transmitral Doppler evidence of elevated LV filling pressures, but is a more powerful prognostic indicator. This is in keeping with previous data demonstrating that E/E' is better correlated with invasive measurement of LVEDP. E/E' was also correlated with Killip class on admission and once more, proved to be a superior predictor of mortality .

Transmitral diastolic flow velocities and DT correlate well with LV filling pressure in patients with impaired LV systolic function but are of limited value in patients with preserved LV systolic function .

In contrast, the E/E’ ratio correlates well with filling pressure, even in patients with a normal LVEF . An E/E' ratio >15 was a significant predictor of an adverse outcome, regardless of LVEF, the presence or absence of ST-segment resolution.

The E/E' ratio was superior to conventional parameters of LV systolic function, such as LVEF and WMSI, for prediction of prognosis. However, it is important to recognize that measurement of E/E' provides complementary prognostic data, with the maximum information obtained by combining this with clinical, systolic, and conventional diastolic parameters.

Interestingly, MR of ≥ 2 + was associated with higher in hospital mortality.

LV dilation and dysfunction affect mitral leaflet competence thereby leading to functional MR. Functional MR in STEMI might be the harbinger of LV dysfunction.

Furthermore, the separation of MR into those with less than grade 2+ and those with grade 2+ or higher provided the greatest discrimination between survivors and nonsurvivors.

Hyperglycemia on admission correlated with poor outcome independently from previous diabetes, as previously reported. Of note, hyperglycemia on admission predicts LV remodeling after first anterior myocardial infarction in non-diabetic patients.

CONCLUSION

Though our results are comparable to the Western data, there is a need to bring down this mortality rate.

The most important clinical prognostic factors of in –hospital mortality are Killip class, age, blood pressure, and heart rate, diabetes mellitus and stress hyperglycemia and prior MI.

In contrast, systemic hypertension with Left ventricular hypertrophy has modestly favorable impact on in –hospital mortality in patients with STEMI. But this findings needs confirmation.

The electrocardiographic characteristics associated with higher in hospital mortality are ST-segment resolution<50%, ST depression in non infarct leads and arrythmias – Complete heart block, high grade AV block, atrial fibrillation , bifascicular blocks, especially RBBB with LPFB.

Bedside 2- Dimensional and Doppler echocardiography provides additional prognostic information over clinical and biological parameters that are routinely determined in patients presenting with STEMI.

Echocardiographic predictors of in –hospital mortality are -

Mitral annular E/E' ratio >15

Mitral Regurgitation > 2+

Left Ventricular ejection Fraction ≤ 30%

Mitral deceleration time (DT) <140 ms

Hypokinesis of non infarct zone

Presence of RV dysfunction

Presence of mechanical complications

In addition, Bedside 2- Dimensional and Doppler echocardiography enables to stratify the high risk group of patients whom may require early revascularization therapy and thus preventing death.

Current guidelines do not recommend index echocardiogram for patients admitted for unequivocal AMI. But recent studies advocate to perform index bedside Doppler echocardiography especially, Tissue Doppler Imaging in the modern era of AMI management.

BIBLIOGRAPHY

1. McGovern PG, Pankow JS, Shahar E, et al. Recent trends in acute coronary heart disease-mortality, morbidity, medical care, and risk factors. The Minnesota Heart Survey Investigators. N Engl J Med 1996;334:884-90.

2. Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The Primary Angioplasty in Myocardial Infarction Study Group. N Engl J Med 1993;328:673-9.

3. Gray D, Keating N, Skene AM, et al. Myocardial infarction in patients over 75 1982-1990. Q J Med 1992;84:659-69.

4. Hospital mortality of acute myocardial infarctionin the thrombolytic era N G Mahon, C O'Rorke,M B Codd, H A McCann, K McGarry, D D Sugrue ;Heart 478 1999;81:478–482

5. Fleming C, D'Agostino RB, Selker HP. Is coronary-care-unit admission restricted for elderly patients? A multicenter study. Am J Public Health 1991;81:1121-6.

6. Goldberg RJ, Samad NA, Yarzebski J, et al. Temporal trends in cardiogenic shock complicating acute myocardial infarction. *N Engl J Med.* 1999; 340: 1162–1168.

7. Goldberg RJ, Gore JM, Alpert JS, et al. Cardiogenic shock after acute myocardial infarction: incidence and mortality from a community-wide perspective, 1975 to 1988. *N Engl J Med.* 1991; 325: 1117–1122

8. European Secondary Prevention Study Group. Translation of clinical trials into practice: a European population-based study of the use of thrombolysis for acute myocardial

infarction. Lancet 1996; 347: 1203-7.

9. Gray D, Keating N, Skene AM, et al. Myocardial infarction in patients over 75 1982-1990. Q J Med 1992;84:659-69.

10. Farnsworth TA. Varying thrombolytic administration rates in elderly patients with acute myocardial infarction. Br J Clin Pract 1993;47:305-7

11. Fleming C, D'Agostino RB, Selker HP. Is coronary-care-unit admission restricted for elderly patients? A multicenter study. Am J Public Health 1991;81:1121-6.

12. SAS User's Guide. 6.08. Cary, NC: SAS Institute Inc, 1989.

13. Behar S, Barbash GI, Copel L, et al. Improved survival of hospitalized patients with acute myocardial infarction from 1981-1983 to 1992 in Israel. The SPRINT Study Group and The Israeli Thrombolytic Survey Group. Secondary prevention Israeli nifedipine trial. Coronary Art Dis 1994;5:1001-7.

14. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000;102: 1788–

15. Kinch JW, Ryan TJ. Right ventricular infarction. N Engl J Med 1994;330:1211–7.

16. Goldberg RJ, Gore JM, Alpert JS, et al. Cardiogenic shock after acute myocardial infarction: incidence and mortality from a communitywide perspective, 1975 to 1988. N Engl J Med 1991;325:1117–22.

17. Berger PB, Ryan TJ. Inferior myocardial infarction: high-risk subgroups. Circulation 1990;81:401–11.

18. European Secondary Prevention Study Group. Translation of clinical trials into practice: a European population-based study of the use of thrombolysis for acute myocardial infarction. Lancet 1996; 347: 1203 -7.

19. Barbash GI, White HD, Modan M, et al. Acute myocardial infarction in the young-the role of smoking.The Investigators of the International Tissue Plasminogen. Activator/Streptokinase Mortality Trial. Eur Heart J 1995;16:313-16.

20. Vlietstra RE, Kronmal RA, Frye RL, et al. Factors affecting the extent and severity of coronary artery discase in patients enrolled in the coronary artery surgery study. Arteriosclerosis 1982;2:208-15.

21. Schor S, Shani M, Modan B. Factors affecting immediate mortality of patients with acute myocardial infarction: a nationwide study. Chest 1975;68:217-21.

22. Handley AJ, Teather D. Influence of smoking on deep vein thrombosis after myocardial infarction. BMJ 1974;iii:230-1

23. de Chillou C, Riff P, Sadoul N, et al. Influence of cigarette smoking on rate of reopening of the infarct-related coronary artery after myocardial infarction: a multivariate analysis. J Am Coll Cardiol 1996; 27: 1662-8.

24. Boden WE, O'Rourke RA, Crawford MH, et al. Outcomes in patients with acute non-Q wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. N Engl J Med 1998;338:1785-92.

25. Yusuf S, Flather M, Pogue J, et al. Variations between countries in invasive cardiac procedures and outcomes in patients with suspected unstable angina or myocardial infarction without initial ST elevation. Lancet 1998; 352:507-14.

26. The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction. Results of the thrombolysis in myocardial infarction (TIMI) phase II trial. N Engl J Med 1989;320:618-27.

27. Guadagnoli E, Hauptman PJ, Ayanian JZ, et al. Variation in the use of cardiac procedures after acute myocardial infarction. N Engl J Med 1995;333:573-8. Antman EM, Braunwald E. Acute myocardial infarction. In: Braunwald E, Fauci A, Kasper D, et al, eds. Harrison's Principles of Internal Medicine. 15th ed. New York, NY: McGraw-Hill; 2001:1395.

28. Alonso DR, Scheidt S, Post M, et al. Pathophysiology of cardiogenic shock: quantification of myocardial necrosis, clinical, pathologic and electrocardiographic correlations. *Circulation.* 1973; 48: 588–596.

29. Menon V, Slater JN, White HD, et al. Acute myocardial infarction complicated by systemic hypoperfusion without hypotension: report of the SHOCK trial registry. *Am J Med.* 2000; 108: 374–380.

30. Cotter G, Moshkovitz Y, Milovanov O, et al. Acute heart failure: a novel approach to its pathogenesis and treatment. *Eur J Heart Fail.* 2002;4:227–234.

31. Cotter G, Moshkovitz Y, Kaluski E, et al. The role of cardiac power and systemic vascular resistance in the pathophysiology and diagnosis of patients with acute

congestive heart failure. *Eur J Heart*

32. Kohsaka S, Menon V, Lange M, et al. High incidence of sepsis complicating cardiogenic shock following acute myocardial infarction. *Circulation.* 2001

33. Rubbo H, Darley-Usmar V, Freeman BA. Nitric oxide regulation of tissue-free radical injury. *Chem Res Toxicol.* 1996; 9: 809–820.

34. Depré C, Vanoverschelde J-L, Goudemant J-F, et al. Protection against ischemic injury by nonvasoactive concentrations of nitric oxide synthase inhibitors in the perfused rabbit heart. *Circulation.* 1995; 92: 1911–1918.

35. Schulz R, Wambolt R. Inhibition of nitric oxide synthesis protects the isolated working rabbit heart from ischemia-reperfusion injury. *Cardiovasc Res.* 1995; 30: 432–439.

36. Ziolo MT, Katoh H, Bers DM. Expression of inducible nitric oxide synthase depresses ß-adrenergic-stimulated calcium release from the sarcoplasmic reticulum in intact ventricular myocytes. *Circulation.* 2001; 104: 2961–2966.

37. Ullrich R, Scherrer-Crosbie M, Bloch KD, et al. Congenital deficiency of nitric oxide synthase 2 protects against endotoxin-induced myocardial dysfunction in mice. *Circulation.* 2000; 102: 1440–1446.

38. Feng O, Lu X, Jones DL, et al. Increased inducible nitric oxide synthase expression contributes to myocardial dysfunction and higher mortality after myocardial infarction in mice. *Circulation.* 2001; 104: 700–704.

39. Godley RW, Wann LS, Rogers EW, et al. Incomplete leaflet closure in patients with papillary muscle dysfunction. *Circulation.* 1981; 63: 565–571.

40. Hillis GS, Moller JE, Pellikka PA, Gersh BJ, Wright RS, Ommen SR, et al. Noninvasive estimation of left ventricular filling pressure by E/e' is a powerful predictor of survival after acute myocardial infarction. J Am Coll Cardiol (2004) 43:360–7

41. Pozzoli M, Capomolla S, Sanarico M, Pinna G, Cobelli F, Tavazzi L. Doppler evaluations of left ventricular diastolic filling and pulmonary wedge pressure provide similar prognostic information in patients with systolic dysfunction after myocardial infarction. Am Heart J (1995) 129:716–25

42. Temporelli PL, Gianuzzi P, Nicolosi GL, Latini R, Franzosi MG, Gentile F, et al. Doppler derived mitral deceleration time as a strong prognostic marker of left ventricular remodeling and survival after acute myocardial infarction: results of the GISSI-3 echo substudy. J Am Coll Cardiol (2004) 43:1646–53.

43. Moller JE, Sondergaard E, Seward JB, Appleton CP, Egstrup K. Ratio of left ventricular peak E-wave velocity to flow propagation velocity assessed by color M-mode Doppler echocardiography in first myocardial infarction: prognostic and clinical implications. J Am Coll Cardiol (2000) 35:363–70.

44. Nagueh SF, Mikati I, Kopelen HA, Middleton KJ, Quinones MA, Zoghbi WA. Doppler estimation of left ventricular filling pressure in sinus tachycardia. A new application of tissue doppler imaging. Circulation (1998) 98:1644–50.

45. Agricola E, Galderisi M, Oppizzi M, Melisurgo G, Airoldi F, Margonato A. Doppler tissue imaging: a reliable method for estimation of left ventricular filling pressure in patients with mitral regurgitation. Am Heart J (2005) 150:610–5.

46. Palecek T, Linhart A, Bultas J, Aschermann M. Comparison of early diastolic mitral

annular velocity and flow propagation velocity in detection of mild to moderate left ventricular diastolic dysfunction. Eur J Echocardiogr (2004) 5:196–204.

47. Perez de Isla L, Zamorano J, Quezada M, Almeria C, Rodrigo JL, Serra V, et al. Prognostic significance of functional mitral regurgitation after a first non-ST-segment elevation acute coronary syndrome.Eur Heart J (2006) 27:2655–60.

48. Ennezat PV, Marechaux S, Asseman P, Lejemtel TH, Van Belle E, Bauters C, et al. Functional mitral regurgitation and chronic heart failure. Minerva Cardioangiol (2006) 54:725–33.

49. Hillis GS, Moller JE, Pellikka PA, Bell MR, Casaclang-Verzosa GC, Oh JK. Prognostic significance of echocardiographically defined mitral regurgitation early after acute myocardial infarction. Am Heart J (2005) 150:1268–75.

GLOSSARY OF ACRONYMS

CAD	Coronary Artery Disease
ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
STEMI	ST Elevation Myocardial Infarction
CS	Cardiogenic Shock
CCU	Coronary Care Unit
CABG	Coronary Artery Bypass Graft
ICD	International classification of diseases
ISIS	International study of infarct survival
GUSTO	Global utilization of streptokinase and tissue plasminogen activator for occluded coronary arteries
MONICA	Multinational monitoring of trends and determinants in cardiovascular Disease
OASIS	Organization to assess strategies for ischemic syndromes
PCI	Percutanous Coronary Intervention
SHOCK	SHould we emergently revascularize Occluded Coronaries in cardiogenic shocK?
TAMI	Thrombolysis and angioplasty in myocardial infarction
TIMI	Thrombolysis in myocardial infarction
VANQWISH	Veterans Affairs non-Q wave infarction strategies in hospital